REMARKS ON THE FUNCTIONS OF THE BASAL GANGLIA *

J. PURDON MARTIN
M.A., M.D. Belf., F.R.C.P.
CONSULTING PHYSICIAN TO THE NATIONAL HOSPITAL FOR NERVOUS DISEASES, QUEEN SQUARE, LONDON, W.C.1

THE great interest aroused by the extension of surgery to the basal ganglia makes it appropriate to review what knowledge we have of the physiological functions of these structures—and, incidentally, how it has been acquired—and the new operations that are being practised present an opportunity, and indeed a challenge, to try to extend that knowledge.

Anatomy

The ganglia that my remarks will be concerned with are the globus pallidus or pallidum, the striatum (by which I mean the putamen and caudate nucleus), the subthalamic nucleus or corpus Luysii, and the substantia nigra. The internal capsule separates them into two pairs, the first two (the larger ganglia) on its outer side, and the smaller ones lying against it medially.

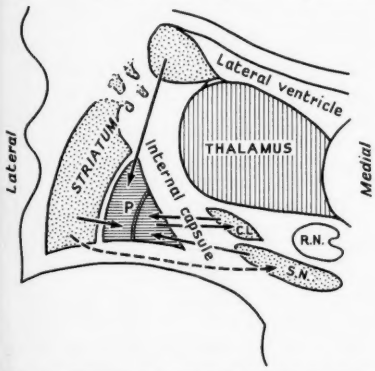

Fig. 1—Diagram of a vertical section to show the relationship of the globus pallidus (P.) to the striatum, corpus Luysii (C.L.) and substantia nigra (S.N.), and the fibre connections within this group of ganglia. R.N., red nucleus.

The fibre connections indicate that these four ganglia form a group, of which the globus pallidus is the centre (fig. 1). Both parts of the striatum send their efferent fibres into the globus pallidus. The corpus Luysii has a strong to-and-fro connection with the globus pallidus; it sends few fibres elsewhere but may send some down into the substantia nigra, and it is believed also to make a contact with its fellow of the opposite side. The substantia nigra is connected with the globus pallidus by numerous fibres some of which cross the internal capsule obliquely, and others pass around and among the fibres of the basis pedunculi. Ranson and Ranson (1941) found in the monkey that all these fibres appeared to be running from the substantia nigra to the pallidum and none in the reverse direction, and observations on human material which are in keeping with this have recently been made at the National Hospital by Dr. Marion Smith; but whether any of these fibres do run in the reverse direction is a matter for further study. A direct connection between the striatum and the substantia nigra has also been described (Rundles and Papez 1937), and this too awaits confirmation.

The fibres that I have referred to so far, provide domestic connections within the group of nuclei. The globus pallidus, however, gives other—longer—efferent fibres which emerge from the group (fig. 2). These are contained in two bundles—a more direct (medial) one, the fasciculus lenticularis, whose fibres pass through the internal capsule, and a less direct (anterior) one, the ansa lenticularis, which takes a longer course and loops round the front of the capsule. The two bundles come together and end in the ventral part of the thalamus.

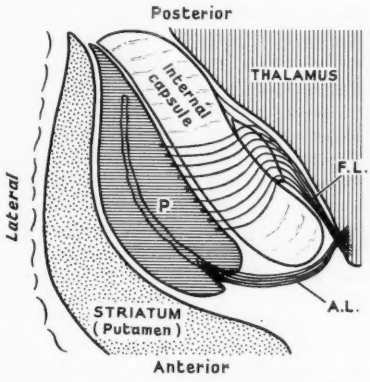

Fig. 2—Diagram of a horizontal section to illustrate the "long" efferent fibres of the globus pallidus. F.L., fasciculus lenticularis; A.L., ansa lenticularis. Both these bundles of fibres end in the ventral part of the thalamus.

We need not concern ourselves much with the fibres that enter this group of nuclei from other parts of the brain, because when we come to discuss their functions we must accept them as influenced by other structures. However, undoubtedly the most important afferent connections of the group come directly or indirectly from the cerebellum.

Difficulties in Discovering Function

The basal ganglia have been very obstinate in concealing their functions. Until recently they have resisted all the usual neurological and physiological methods of discovering them. Stimulation or destruction of individual ganglia in different kinds of animals presented many difficulties, and until a few years ago such methods seldom gave any positive results, or when they did so, later experimenters failed to confirm them. But neurology's traditional method of investigation by which so much of our knowledge of brain function has been acquired depends on clinical and pathological observation, and the clinico-pathological method has encountered peculiar difficulties in dealing with the basal ganglia. In the first place, the method depends on the occurrence of circumscribed lesions, and practically all the diseases which have symptoms of the kind that we attribute to dysfunction of the basal ganglia are diffuse pathological conditions—such as Wilson's disease, Huntington's chorea, and postencephalitic parkinsonism—and with such widespread pathology no conclusion can be drawn as to the function of this or that ganglion. Secondly, when local lesions do occur from disease, they are not often helpful for investigational purposes: vascular lesions and secondary tumours in the lenticular and caudate nuclei are not uncommon, but we do not recognise any symptoms resulting from them. The third, and undoubtedly the greatest, impediment to the use of the clinico-pathological method lies in the nature of the symptoms themselves.

The symptoms that we have learnt by experience to

* From lectures given to the Montreal Neurological Society (May, 1958) and at the National Hospital, Queen Square.

attribute to disease of the basal ganglia are all of a *positive* nature (tremor, involuntary movements, excess of muscle tone): they involve an excess of activity—an expenditure of energy—and such symptoms cannot arise directly from destruction of cerebral tissues. The pathological picture may show what structures are diseased and partly destroyed, but it does not show which of the surviving structures are responsible for the involuntary movements or excess of tone.

The clinico-pathological method has, in fact, made several false starts, so to speak, each of which has seemed hopeful at first, and then petered out. As long ago as 1874 and 1876 Benedikt described two cases in each of which a lesion in one half of the midbrain involving the red nucleus, and of course the oculomotor nerve, was associated with tremor of the limbs on the opposite side of the body. The tremor was subsequently attributed to destruction of the red nucleus, and it was Charcot who proposed that the condition, with the ocular palsy on the side of the lesion, should be called " Benedikt's syndrome "—the name it has since borne. This was a most important observation, and time has not diminished its significance; but the exact structure, damage to which gives rise to the tremor, has proved peculiarly hard to identify. After a long period of conflicting evidence physiologists now tell us that lesions limited to the red nucleus in the monkey do not cause tremor, but lesions beside it may do so; and no-one knows to this day whether or not tremor arises as a result of destruction of the red nucleus (or of part of the red nucleus) in the human subject.

Nearly twenty years after Benedikt's publication of his cases, Blocq and Marinesco (1893) described the pathology of a case with a left hemiparkinsonian syndrome, the clinical notes of which had been taken by Maître Charcot himself. They found a tuberculoma in the right half of the midbrain, destroying the substantia nigra and evidently part of the red nucleus, together with the intervening structures. While this case has considerable physiological importance, the fact that the lesion was not limited to a single structure prevented any precise conclusions being drawn as to the origin of tremor or rigidity, and moreover no confirmatory cases were described.

About another twenty years passed, and in 1912 Kinnier Wilson published his masterly, and now classical, description of the disease which bears his name and which he called " progressive lenticular degeneration ". In his cases the putamen, particularly, was severely degenerated, even to the extent of cavitation, and Wilson, not unnaturally, attributed the symptoms of muscular rigidity and abnormal movements to this degeneration. But Wilson himself, when he went on to experimental work (1914), had the disappointment of finding that even large lesions in the lenticular nuclei of primates gave rise to no recognisable symptoms, and certainly nothing comparable to those of the disease which he had just described; and so, physiological advance was again frustrated.

Two Disorders of Function

1. HEMICHOREA (HEMIBALLISMUS)

Eventually clinico-pathological observation did achieve a success. By the end of another twenty years after Wilson's paper, a good deal of interest was being taken in another structure, to which hitherto little attention had been given—namely, the subthalamic nucleus or corpus Luysii. By that time quite a number of cases had been described in which small lesions, more or less destroying this structure, and more or less limited to it, had been associated during life with a severe hemichorea—often called " hemiballismus "—of the opposite half of the body.

Hemiballismus does not differ from hemichorea except perhaps in severity. I shall use the term to apply exclusively to those cases in which there is reason to believe that the hemichorea results from a lesion of the corpus Luysii or its efferent fibres. Hemiballismus seems to me a pure syndrome of involuntary movements, though admittedly it may be associated with some diminution in muscle tone in the affected limbs. Most other syndromes of involuntary movements are complicated by some degree of muscular rigidity or signs of pyramidal disturbance. The movements of hemiballismus go on all the time as long as the patient is awake and they cease entirely during sleep. The patient remains able to make voluntary movements and to direct his movements, within limits, so that, choosing his moment, he can, for instance, make the precise movement of touching his nose with his index finger. In other words, underneath the involuntary movements, voluntary movement remains intact.

Reports of such cases continued to accumulate. In 1927, when describing such a case (Martin 1927), I had been able to find about a dozen instances in the literature, going back to 1880. In 1934 Martin and Alcock, describing another case, were able to refer to 21 published similar cases. In 1947, Whittier wrote a review including 30 cases of this kind collected from the literature, every one of course with post mortem confirmation of the lesion, and in 1953 Yvette Martinez in her thesis reviewed 53 such cases and added 2 new ones from Garcin's clinic. Meanwhile, no case had, to my knowledge, been described in which an isolated lesion of the corpus Luysii was not associated with hemichorea.

The condition had for some time been ripe for experimental investigation when, in 1949, Whittier and Mettler, and afterwards Carpenter, Whittier, and Mettler (1950), published their findings in an extensive series of experiments on monkeys. Using a stereotactic technique, they made lesions which destroyed or involved the corpus Luysii, and found that " choreoid hyperkinesia " of the opposite side of the body regularly resulted, provided (1) that the lesion destroyed at least 20% of the volume of the nucleus, and (2) that it was not so large as to damage certain other structures. " Destruction of the greatest volume of nucleus associated with the least involvement of other structures provoked the most violent 'choreoid hyperkinesia' ".

I think it may therefore be regarded as established that destruction of the corpus Luysii in some way gives rise to hemichorea (hemiballismus) affecting the opposite side of the body. Here, for the first time, it seems that we have a site in the basal ganglia at which a local lesion gives rise to a constant and obvious effect. This provided a starting-point for further physiological investigation.

Before I leave this part of the subject I think I should point out that not all chorea is associated with significant disease of the corpus Luysii. Huntington's disease provides the best example of the contrary, and we should notice in passing that in that condition the striatum usually suffers severely.

The Other Side of the Problem

Now, it is evident that a destructive lesion cannot of itself give rise to " positive " symptoms. The choreic movements must depend on irregular impulses entering

the motor system; and clearly such impulses cannot arise from destroyed tissue, but must be coming from some cells that are still intact and must be transmitted along fibre pathways which also are still intact. Kinnier Wilson frequently insisted on this point: he called it a platitude and it is obvious when expressed; but it is very apt to be forgotten, and a good deal of confusion has occurred from a failure to keep it clearly in mind. It was partly because of Kinnier Wilson's attitude that Martin and Alcock (1934) were very explicit on this aspect of the matter:

" If however we could determine that damage to certain structures, without gross involvement of any others, uniformly gave rise to chorea, we would then be in a position to investigate the subject from the other side and endeavour to determine what structures must be intact in order that chorea may occur. . . . Where do the abnormal impulses arise? By what paths do they travel? In what functional system do they exist? " and so on.

We cannot pursue all these questions now, but here, obviously, was the next stage of the inquiry. What structures must be intact?

The observation had already been made that large lesions, even though they engulfed the corpus Luysii, did not give rise to hemichorea; and so it was deduced that some structure (or structures) not too far distant from the corpus Luysii was (were) essential to the occurrence of the abnormal movements. Carpenter, Whittier, and Mettler quickly found that this structure was the neighbouring globus pallidus, or, alternatively, its efferent fibres in the lenticular fasciculus. One of their conclusions in their paper of 1950 was expressed as follows: " Choreoid hyperkinesia was eliminated or reduced in violence and persistence unilaterally by destruction of appropriate volumes of the globus pallidus contralateral to the symptom." Other conclusions were:

" Lesions that provoked unequivocal choreoid hyperkinesia were contralateral to the symptom and involved preservation of the integrity of adjacent structures, particularly the lenticular fasciculus and the internal segment of the globus pallidus."

" Lesions which produced (only) moderate and/or non-persistent choreoid hyperkinesia usually damaged parts of the lenticular fasciculus or internal segment of the globus pallidus."

Carpenter, Whittier, and Mettler drew the conclusion that

" integrity of the pallidum and the lenticular fasciculus is necessary for the maintenance of the neural mechanism responsible for choreoid hyperkinesia resulting from lesions in the sub-thalamic nucleus ".

We would hardly be justified in deducing at this stage that the impulses responsible for the involuntary movements arise primarily in the globus pallidus, but we are justified in concluding that *the globus pallidus provides something which is essential for the occurrence and persistence of the movements.*

So much for hemiballismus for the moment! In regard to one kind of disturbance of function of our group of ganglia we have discovered (*a*) a local lesion that will bring it on, and (*b*) a local lesion that will abolish it. A ganglion has been identified in which a lesion gives rise to a " positive " effect and another has been identified in which a lesion then causes a " negative " effect. That was the position after 1950.

A Turning-point

It should be noted in passing that this represents a turning-point in our knowledge of the functions of the basal ganglia. For the first time a localised destructive lesion in these ganglia produced an obvious " negative " effect; for the first time it was clearly seen to abolish an activity. All the recent surgical intervention in the basal ganglia depends on the fact that when " positive " symptoms are present such a " negative " effect can be obtained. Secondly, a site or sites had been identified at which a destructive lesion would produce such an effect on one particular activity.

2. MUSCULAR RIGIDITY

Now let us turn to the surgical contribution.

You may not all have seen hemiballismus but you are all familiar with the muscular rigidity of the parkinsonian syndrome. Increasing hypertonus affects all the muscles of one side or both sides of the body and impedes voluntary movement to such a degree that the patient eventually becomes imprisoned in the rigidity of his own muscles. This lasts throughout the day but the muscles relax when the patient is asleep and possibly he may remain relatively relaxed for a short time after he wakens up. Quite a number of years ago Walshe showed that if the rigidity was temporarily abolished, the patient could make quite quick and normal voluntary movements; so, as with hemiballismus, voluntary movement remains unimpaired underneath the abnormality.

Some eight or ten years ago surgeons began to tell us that this muscular rigidity of the parkinsonian syndrome (and often the tremor too) could be relieved or abolished by destructive lesions in the globus pallidus (Spiegel and Wycis, Cooper), or by interruption of the pallidofugal fibres (Fénélon, Meyers) and more recently by partial destruction of the end-station of these fibres in the ventral nuclei of the thalamus (Hassler and Reichert). As far as I know, Russell Meyers in America, and Fénélon in France, were the pioneers of operations in the field of the basal ganglia.

Our knowledge of the pathological background of this hypertonus or muscular rigidity is less exact than our knowledge of the pathological background of hemichorea. Whether a local lesion can cause it or not we do not know. However, in a number of cases of postencephalitic parkinsonism in which muscular rigidity was the only recognised symptom, the cells of the substantia nigra were found to be completely degenerated, and even in idiopathic Parkinson's disease these cells suffer considerably. In other diseases too the same association is found between the syndrome of rigidity and degeneration of the substantia nigra (Biemond and Sinnege 1955). I have not been able to find any clinico-pathological description of a satisfactory case in which the symptoms were attributed to a local lesion limited to the substantia nigra; the case of Charcot, reported by Blocq and Marinesco, is the best we have; and that, though important, is obviously imperfect. We have no experimental evidence that destruction of the substantia nigra gives rise to muscular rigidity; in fact, we are told that in the monkey it produces no recognisable effect (Mettler 1957). There may, therefore, be another factor; or there may be contrary factors in the animal experiments; but we can at least say from clinico-pathological evidence that degeneration of the substantia nigra is compatible with muscular rigidity and often accompanies it.

Not all " extrapyramidal " rigidity is associated with significant disease of the substantia nigra. Wilson's disease provides the best example of the contrary, and

again, we should notice in passing, that in this condition the striatum suffers severely.

All that I have said about the association of a destructive lesion with a positive symptom applies, of course, just as much to muscular rigidity as to hemichorea. In the same way there is another side to the problem—the positive symptom is due to the activity of surviving structures. What structures must be intact in order that rigidity may occur? So far, there is relatively little pathological evidence that the operative lesions which abolish rigidity are limited to the globus pallidus and its efferent fibres; but such evidence is accumulating and moreover the different operations are consistent among themselves. Accepting the surgical evidence as valid, it appears that the pallidum and its efferent fibres must be intact for rigidity to occur—that the activity of the pallidum is necessary for the maintenance of rigidity, as we saw it was for hemiballismus.

Thus, with reservations, we can say of this disturbance of function that a degeneration of the substantia nigra is associated with a " positive " effect, and a lesion in the globus pallidus then produces a " negative " effect.

It is, however, necessary to mention the possibility that the degeneration of the substantia nigra may not be the equivalent of a purely destructive lesion, but that in the process of degeneration of the cells a " discharging lesion " may arise. Such discharging conditions may persist for a very long time. This could have either a stimulating or an inhibitory effect on the globus pallidus according to which action the substantia nigra normally exerts, and a stimulating effect might account for muscular rigidity. This would not materially alter our view of the relation of rigidity to the globus pallidus, but it would alter our view of the action of the substantia nigra.

That the effect of the degeneration in the substantia nigra is of this nature seems to me very unlikely, because the discharging condition is associated with an early stage of degeneration of cells, whereas what is found in the substantia nigra in association with severe rigidity is merely the debris resulting from complete break up of the cells: the rigidity is at its most severe when most of the cells of the substantia nigra are long past any possibility of discharge. This theory therefore appears to me inconsistent with the facts and I shall not refer to it further.

The Parts Played by Individual Nuclei

These disorders show that the group of ganglia we are considering contains a mechanism or mechanisms concerned with muscular activity, and it will be helpful to discuss briefly at this stage the parts played under different circumstances by the individual nuclei of the group.

Globus Pallidus

The two disturbances of group function that we have considered are characterised by an excess of activity—by an excessive discharge of energy—and the action of the globus pallidus is evidently necessary for both of them. By far the most important connections of the corpus Luysii are those with the globus pallidus; and I think we are bound to infer that when the corpus Luysii is damaged the globus pallidus is the nucleus whose function will be most disturbed. Hemiballismus is evidence of very irregular impulses and I do not see any other explanation than that these irregular impulses emanate from the globus pallidus. They are the product of its disturbed function, and presumably under more normal conditions these impulses are regulated. The argument from muscular rigidity is a little less firm, but leads similarly to the conclusion that the globus pallidus is the source of the continuous excessive discharge which must be required to maintain the constant muscular activity.

Therefore in both these disorders, which are very different, we see the globus pallidus as a source of nervous impulses and in a state of continuous activity as long as the subject is awake.

[In spite of this, as we shall see later, evidence of any such activity under normal circumstances is conspicuous by its absence.]

Corpus Luysii

We saw that the globus pallidus was necessary for the occurrence of hemiballismus, and the recent surgical operations show us that it is necessary for the occurrence of rigidity. We must not deduce from this that the globus pallidus has two different kinds of activity—one for hemiballismus and the other for muscular rigidity. It is a simple structure with only one kind of nerve-cell, and it is unlikely to have more than one kind of activity. The difference in the symptoms for which it is partly responsible results from the difference in the nuclei with which it is associated in the two instances. When the corpus Luysii is destroyed the resulting activity of the group of nuclei, as expressed in muscular activity, is very irregular; when the corpus Luysii is intact the activity—both in the normal state and in the case of rigidity—is continuous and uniform. The deduction seems to be warranted that the corpus Luysii in some way controls and modulates the activity of the globus pallidus, and that relative integrity of it is necessary for a uniform activity of the latter.

Substantia Nigra

Degeneration of the substantia nigra is associated with muscular rigidity, but I have said only that this degeneration is compatible with rigidity. The clinico-pathological association, however, is very close, and it has been accentuated by the description by Biemond and Sinnege (1955) of an hereditary form of parkinsonism characterised clinically by rigidity (without tremor), and pathologically by an intense degeneration of the substantia nigra, all the other basal ganglia being intact. Unless we can find a " cause " of this kind of rigidity outside our group of ganglia, we must accept that it is due to the degeneration of the substantia nigra—that degeneration of the substantia nigra is a " cause " of rigidity in the same sense as destruction of the corpus Luysii is a " cause " of hemichorea, and not merely a chance finding associated with it.

Rigidity, being a positive symptom—a sign of excess of function—cannot be directly due to the degeneration of cells in the substantia nigra; it is due, as I have argued, to excessive activity of the globus pallidus (in association with the corpus Luysii); degeneration of the substantia nigra can be a " cause " of rigidity only in the sense that it permits such excessive activity of the globus pallidus. This leads us to the further conclusion that in normal circumstances the intact substantia nigra must have an inhibitory effect on the action of the globus pallidus (as influenced by the other ganglia).

The Striatum

The striatum is bigger than the other three nuclei put together. It has been in the background all the time, but nothing that I have said about hemiballismus or rigidity throws much light on its function, and we must look for indications elsewhere.

Evidence about the function of one structure from diffuse disease is, of course, suspect; but in association

with what we know about the function of other ganglia it may have some value. The putamen and caudate nucleus are often extensively degenerated in Huntington's chorea, and the putamen above all, in Wilson's disease: both of these diseases are characterised by pronounced " positive " symptoms, and this evidence, as far as it goes, suggests that the striatum belongs to the " controlling " group of nuclei rather than reinforces the action of the globus pallidus. This is in keeping with the conclusion reached by Mettler from earlier experimental work that the striatum has an inhibitory effect on the pallidum (Mettler 1942, 1957). We know from clinico-pathological and experimental evidence that isolated lesions in the striatum produce no recognised symptoms—i.e., when the other ganglia are intact they produce neither negative symptoms nor positive symptoms. Such evidence is, however, inconclusive, because, the striatum being a very large structure, a single lesion big enough to destroy any considerable fraction of it is likely to involve other structures as well, and particularly to involve the globus pallidus, and thereby prevent positive symptoms.

The striatum (" neostriatum ") is phylogenetically a newer structure than the pallidum. From what we know of other phylogenetically newer structures—the " neocortex " and the " neocerebellum "—we must suppose that it would produce an elaboration and refinement of the action of the structures with which it is associated, and so possibly represent a " higher control " within the group. It may be of significance that the symptoms of the diseases in which it is severely degenerated are similar to the symptoms associated with degeneration of the older " controlling " nuclei in the group. Histologically, the striatum is a more complex structure than the other ganglia we have considered and its action may well be mixed. For the time being, therefore, the striatum still obstinately conceals its function; but I think we have enough evidence—clinico-pathological and experimental—to warrant the general conclusion that its action is of an inhibitory or controlling character.

The Basis of Symptoms in General

The functional arrangement of the group, then, is that of a dynamic central ganglion, the globus pallidus, surrounded by three controlling ganglia.

An appropriate lesion of any of the controlling ganglia, the globus pallidus being relatively intact, will give rise to a " positive " symptom; and considering the size and number of the controlling nuclei it is not surprising that " positive " symptoms are usual.

It is not quite right to regard such symptoms as " release phenomena "; they should all rather be regarded as disturbances of the function of the group of ganglia as a whole. Muscular rigidity, for instance, may be indirectly due to degeneration of the substantia nigra; but it is more directly due to the activity of the globus pallidus, in association with the corpus Luysii and the striatum. Similarly, hemiballismus may be due indirectly to destruction of the corpus Luysii; but it is more directly due to the activity of the globus pallidus as influenced by the substantia nigra and the striatum. For just such a conception as this, Hughlings Jackson coined the phrase " physiology in difficulties ", which Kinnier Wilson also made use of.

I have confined myself to the discussion of pure syndromes; but, of course, combined syndromes of involuntary movements and rigidity are more common, and must be held to arise (indirectly) in the same way, from lesions of the controlling ganglia with relative integrity of the globus pallidus.

" Negative " symptoms might be expected to arise from lesions of the globus pallidus. Actually, as far as I am aware, no motor deficiency symptoms have been observed in clinical cases from lesions limited to this ganglion. Moreover in experimental work, Wilson and others have failed to observe any disabilities resulting from lesions placed in the pallidum. It may be that under normal circumstances the globus pallidus is completely held in check and that a weakening of its activity, as a result of organic damage, simply swings the balance in favour of the controlling group and does not produce any symptom. This is a matter for further observation; but such a state of balance in the system would account, on the one hand, for the ready occurrence of positive symptoms with disease of the controlling nuclei, and, on the other hand, for the absence of negative symptoms with lesions of the globus pollidus.

These are probably not the only ways in which symptoms may arise. I have refrained from making any reference to tremor—and that for two reasons, which perhaps merge into one. In the first place I could not find in the group of ganglia I have been speaking of, any local lesion which gave rise to tremor, and secondly, those sites in the central nervous system at which lesions seem to produce tremor are outside this group of ganglia. However, parkinsonian tremor does seem to be due to a disturbance of the function of these ganglia and may be abolished, as we shall see, by operative lesions affecting the globus pallidus. I do not propose to discuss this, beyond pointing out that Benedikt's syndrome provides the suggestion that tremor may arise in consequence of a lesion of fibres afferent to the basal ganglia. This view has been advocated particularly by Mettler on the basis of experimental work and seems to me to provide an acceptable hypothesis for a matter on which clinical evidence is scanty.

Whether, similarly, any symptoms may arise from disturbances along the efferent pathways (still largely speculative) which these impulses traverse between the globus pallidus and the muscles, is a question on which, as far as I know, there is no good evidence.

The Effects of Operations

When operations on the basal ganglia came into vogue, the techniques by which the lesions were made were various, but almost always the surgical procedure was directed towards the globus pallidus, or in some cases towards its efferent fibres. While there were, and are, many satisfactory results, these operations often gave incomplete relief of the symptoms. Irving Cooper (1956) estimated his proportion of worth-while results at 65–70%. The success of this operation probably depends on weakening the action of the globus pallidus so as to bring it again under the dominance of the controlling ganglia.

The operation which has interested me more is one which places a lesion at (or near) the ventral portion of the thalamus. This operation (as can be appreciated from fig. 2) must interrupt all the pallido-thalamic fibres—both those in the fasciculus lenticularis and those in the ansa—and thus block the whole outflow of impulses from the globus pallidus (with the possible exception of some to the hypothalamus, or its neighbourhood). It is capable of completely abolishing hemiballismus (Martin and McCaul 1959) and of completely abolishing muscular rigidity (and tremor too) in the limbs of the opposite side of the body.

Our previous discussion had led us to the belief that the globus pallidus in pathological conditions, was a very active ganglion. Now, when its action is completely blocked (at least as far as muscular activity is concerned) the surprising thing is that no defect of normal function is apparent in the previously affected limbs; nor is the patient aware of any disability. I am speaking, of course, of the most fortunate results. The power and coordination of voluntary movement are normal; there is no appreciable slowness in the initiation of movement; the patient does not complain of any loss of spontaneity of movement, nor of any fatigue in the affected limbs; " associated movements " such as the swinging of the arm in walking appear to be normal; the tone of the muscles feels normal; the arm is normally sustained for the execution of fine movements by the fingers and hand; and the position of the outstretched hands remains normal when the patient's attention is distracted. Whatever the normal function is which has been abolished it is one that can quite well be done without.

The Basal Gangliar Mechanism

What physiological deductions are we entitled to make from these facts? I have already referred to the parts played by the individual nuclei, and it remains to say something of the function of the group as a whole.

I mentioned that when muscular rigidity was abolished by an operation, normal muscle tone remained in the previously affected limbs. Obviously, then, the mechanism which has been interfered with by the operation is one for the production of *additional* muscle tone—a supplementary tone-producing mechanism.

It is true that in some pathological conditions the mechanism gives rise to involuntary movements; but under physiological conditions—with the corpus Luysii and the striatum acting normally—the evidence we have indicates that the muscular activity will be of a smooth, uniform character. The normal mechanism would seem to be one for uniform or tonic muscular action, but capable probably (e.g., with changes in the activity of the corpus Luysii) of sudden changes of activity sufficient to produce movement.

Like various other mechanisms in the central nervous system, this mechanism exhibits its activity only under pathological circumstances.

It is evidently not in any way necessary for voluntary movement. Neither is it necessary for the " associated " movement of swinging the arm in walking. Finally, as I have said, the results of operation show that it can quite well be done without. However, this is not to say that it is not made use of when it is available.

The difficulty in discovering any defect of function when the basal gangliar mechanism is blocked (by operation) makes it more difficult for us to discover its normal action, if any. On the one hand it is possible that it is a mechanism which has been superseded in the course of cerebral development and has ceased to have any normal function. On the other hand, as I have suggested, it may under normal circumstances be in a state of balance, so that all " positive " activity is checked; and yet, such a state would both make it more sensitive to the varying activity of the controls and hold it ready to be brought into operation in special circumstances.

Conclusion

The present picture, then, of this group of ganglia is that of a dynamic central nucleus, the globus pallidus, surrounded by three controlling nuclei. The group contains a supplementary mechanism for muscular action, chiefly of a tonic type, the effects of whose activity are so far recognisable only under pathological conditions. Disorders of this mechanism give rise to involuntary movements and muscular rigidity.

We have succeeded in unravelling to some extent the pathological activities of the group, and the challenge which now confronts us is to discover under what physiological conditions the mechanism which the group contains is called into play. It might be said that this mechanism has a great capacity for evil—and thereby it reveals itself—but its capacity for good has yet to be discovered.

Summary

1. The globus pallidus, the striatum, the corpus Luysii, and the substantia nigra should be regarded as a group. A disturbance of one of these nuclei cannot profitably be considered in isolation, but should be considered in relation to the group as a whole.

2. The two disorders which we have mainly considered interfere with voluntary movement by maintaining continuous excessive muscular activity, but the capacity for voluntary movement is intact underneath the excessive activity. While, therefore (a) the action of *the group* is evidently concerned with muscular activity, (b) it seems unlikely to be immediately concerned with voluntary movement.

3. (a) The anatomical arrangements suggest that the group acts through the *globus pallidus*. (b) A lesion of the globus pallidus or of its efferent fibres has a negative effect which may abolish pre-existing positive symptoms; taking this in conjunction with the anatomical arrangements, I do not see any other explanation than that the impulses exciting the positive symptoms emanate from the globus pallidus. (c) The positive symptoms are continuous as long as the subject is awake, and so the globus pallidus in these pathological circumstances is evidently in a state of constant activity throughout the waking hours. (d) However, when the action of the globus pallidus is blocked by interruption of its efferent fibres, no defect of function is apparent in the limbs previously the seat of positive symptoms.

4. (a) When the *corpus Luysii* is damaged by an isolated lesion, the impulses from the globus pallidus become excessive and irregular, and involuntary movements occur (hemiballismus). The deduction seems to be warranted that the corpus Luysii acts in some way as a controller and modulator or monitor of impulses from the globus pallidus. (b) Degeneration of the *substantia nigra*, the corpus Luysii being more or less intact, is associated with excessive muscular tone leading to rigidity of the contralateral limbs; probably in the normal state the substantia nigra has a direct or indirect inhibitory action on the activity of the globus pallidus. (c) Such evidence as we have about the function of the *striatum* (putamen-caudate) indicates that it, too, is of an inhibitory or controlling character.

5. The group contains a mechanism for muscular activity, chiefly of a tonic type; but in ordinary circumstances this mechanism can quite well be done without, and we have yet to discover under what physiological circumstances it comes into action. Disorders of this mechanism give rise to involuntary movements and muscular rigidity.

I am greatly indebted to my surgical colleagues at the National Hospital, and to Mr. Ian McCaul, of the neurosurgical unit at the Whittington Hospital, who have made me free to study their cases

before and after stereotactic operations. I also had the benefit of seeing a large number of patients demonstrated by Dr. Irving Cooper at a symposium in New York in May, 1958.

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FLOCCULATION TESTS

GEORGE DISCOMBE
M.D., B.Sc. Lond.
PATHOLOGIST, CENTRAL MIDDLESEX HOSPITAL, LONDON, N.W.10

THE flocculation tests commonly called "liver-function tests" depend mainly on changes in the serum-proteins, and most of them give abnormal results in a variety of diseases whose only common factor is that serum-protein levels are disturbed. Those used today are the survivors of a host of flocculation tests devised between 1917 and 1947 to simplify the diagnosis of infectious disease. Their mechanism is now fairly well understood, and it is the purpose of this paper to outline the mechanisms involved and compare the clinical usefulness of these tests so that the minimum of labour need be wasted on unprofitable work.

Most of these flocculation tests depend on the dilution of serum with distilled water or water containing very low concentrations of electrolytes, usually buffers of ionic strength 0·01 and pH between 7·5 and 7·8. Under these conditions the components of γ-globulin which used to be called "euglobulin" are very near their isoelectric point and tend to precipitate. Chorine (1937) showed that the most potent flocculating agent was that fraction of globulin which is precipitated when serum is dialysed against distilled water, and the most potent component of this euglobulin was that fraction which did not dissolve in 0·4% sodium chloride. Henry (1928a) sought to demonstrate antibodies to malarial melanin by flocculating melanin suspensions with serum, but Trensz (1932), Greig et al. (1934), and Wiseman (1934) showed that the melanin merely served to make the fine precipitate of globulin more evident, apparently by entraining the melanin which should be regarded as a passive indicator. Chorine and Gillier (1933a and b) showed that antibodies to melanin could not be made, and they found the reaction to depend mainly on globulin and salt concentration. Henry himself (1928a and b, 1929a–d, 1931, 1933) and Auriccio and Chieffi (1935) replaced melanin by iron albuminate, peptonate or cacodylate and Prudhomme (1935) showed that colloidal particles of melanin carried a negative charge and could be replaced by killed staphylococci or finely divided carmine. Cabello and Miquel (1954) tried a series of colloids and found that any colloid carrying a negative charge could be used as indicator.

Another group of tests depends on the power of various phenols to liberate lipoid from lipoprotein; when the liberated lipoid has formed a colloidal emulsion, this can be flocculated by globulins in the same way as other electronegative colloids. The best known of this group are Maclagan's thymol turbidity test (1944b), extended by Neefe (1946) as a flocculation test; but Vernes' (1929) resorcinol test has been extensively used in France for the diagnosis of tuberculosis, and Kunkel et al. (1948) used phenol in the presence of 12% sodium chloride, a concentration quite high enough to prevent precipitation of "euglobulin".

Historical Summary

Non-colloidal Reagents

Brahmachari (1917) first noted that whereas normal serum gave only slight turbidity when diluted with distilled water, serum from patients with kala-azar gave much greater turbidity. Sia and Wu (1921) showed the precipitate to be globulin, and Ray (1921) used whole blood instead of serum, the red-cell ghosts acting as indicators of protein precipitation (Sia 1921, 1924). Henry introduced his "melano-flocculation" reaction in 1928 as a test for active malaria, but Chorine and Prudhomme (1934) showed that it was positive also in syphilis, and Chorine et al. (1934) noted the very high values in kala-azar and remarked that the dilution test ran parallel with Henry's test; Trensz (1932) and others showed the melanin to be passively agglutinated (see above). Chorine (1937) reviewed this early work and added to the list of "indicators" methylene-blue, phenol-red, and methyl-red. When photoelectric absorptiometers became available these procedures were made more nearly quantitative by Dreyfuss (1948) and Antoniades (1953); both noted that if the diluting fluid were saturated with CO_2, or if CO_2 were blown through it, the precipitate became more abundant.

Vernes made a fairly systematic and detailed survey of flocculating agents with his photometer; Vernes et al. (1929) give a list of 81 reagents which had been tried. Kunkel (1947) used 2 of these, zinc and copper sulphates, in buffered solutions of low ionic strength and found the turbidity correlated well with the γ-globulin content of serum. All the tests mentioned so far correlate well with γ-globulin and are little affected by other globulins or by albumin.

A second group of tests depends on precipitation with heavy metals, notably cadmium (Wunderly and Wuhrmann 1945, 1946) and mercuric mercury, by titration (Gros 1935, Vischer 1941, Grinstead 1948, Verschure 1950, Maclagan, Benondi, and Cooke 1957), by turbidity (Mira and Dusanka 1954), or by observation of precipitation, the Takata-Ara reaction (Gros 1935, Vischer 1941, Hafstrom 1946, Olhagen 1947). The urea-stibamine reaction for kala-azar (Chopra et al. 1927a, b, and c) may belong here. Uranyl acetate precipitates all normal proteins, but leaves in solution some paraproteins which can be precipitated by trichloracetic acid (Dirr and Dietz 1954, Dirr 1955, Heepe et al. 1957), which may be identical with the mucoproteins or seromucoid of other authors (see Discombe 1959). These tests are affected mainly by γ-globulin, but β-globulin may potentiate the precipitation and albumin inhibits it.

Precipitation with non-ionic solvents such as alcohol, though used in the Cohn fractionation of proteins and

applied to quantitative estimation by Pillemer and Hutchinson (1945) has been used little for flocculation tests. Naidu et al. (1942), Waldenstrom (1946), and Love and Mawson (1948) have experimented with them but they have never become popular. All these tests seem to correlate fairly well with γ-globulin, as do the salting-out with ammonium sulphate procedures of de la Huerga et al. (1950) or Levin et al. (1950) which I find less satisfactory than the zinc-sulphate turbidity test, though de la Huerga et al. (1950) find the reverse.

A last group involves gross chemical or physical changes in the protein. The formol-gel reaction of Gate and Papacoustas (1920), thought to be specific for syphilis, depends mainly on γ-globulin; it was applied to kala-azar by Spackman (1921) and Napier (1921) and further studied by Verhagen (1948); Bing (1937) gives the bibliography to that date. Weltmann's (1930) coagulation band and Bauer's (1934) magnesium-chloride reaction involve heating dilutions of serum in presence of calcium and magnesium salts respectively; Olhagen (1947) considers them to depend on the proportions of the various components, γ-globulin increasing, and α-globulin and albumin reducing the precipitation. The iodine reaction of Mallen et al. (1950) falls into this group but is affected also by some non-protein factors (Discombe and Duggan 1956).

Colloidal Reagents

Lyophobic colloids have a sharp discontinuity between particle and medium; such are the cephalin-cholesterol emulsion and colloidal gold. Lyophilic colloids have no such sharp boundary and exist as hydrated micelles; such are proteins and many dyestuffs of high molecular weight. Some of the indicators used in the dilution test are actually colloids (melanin, carmine, iron peptonate) and others are on the border between colloid and crystalloid (methylene-blue). Cabello and Miquel (1954) pointed out that colloids carrying a positive charge were of no use as indicators, but the whole series of negatively charged colloids, lyophobic and lyophilic alike, could be used in flocculation tests to give almost identical results; they studied six colloids in detail and found them to agree closely with the colloidal gold (Bauer 1937, Gray 1940, Maclagan 1944b, 1946) and colloidal red (Maizels 1946, Ducci 1947) tests; these were colloidal benzoin (Fischer and Wiltner 1949), gum gutta, colloidal silver, copper ferrocyanide, indian ink, and "Poirrier's blue" (triphenyl rosaniline sodium sulphonate which is alkali blue 6B, colour-index number 703). The flocculation of any of these depends on:

(1) Concentration of serum and colloid.

(2) pH: normal serum flocculates only on the acid side of pH7·2; pathological serum flocculates maximally at pH 7·8 but becomes inactive above pH 8·4. This agrees with the effect of CO_2 as noted by Dreyfuss (1948), Antoniades (1953), and Discombe, Jones, and Winstanley (1954).

(3) The concentration of electrolytes which diminish flocculation at concentrations greater than 0·015 M (ionic strength 0·015) (see also Chorine 1937, Chorine and Gillier 1933a and b).

(4) The presence of phenol which always increases flocculation, possibly by acidification, more probably by liberation of lipid from lipoprotein.

Among these colloid tests must also be included the cephalin-cholesterol flocculation (Hanger 1939) and shellac (Fischer and Wiltner 1949) tests. Their mechanism has been studied by Moore et al. (1945), Recant et al. (1945), Maclagan and Bunn (1947), Martin (1946), Dekema (1951), Maclagan, Martin, and Lunnon (1952), and Armas-Cruz et al. (1952), as well as by Cabello and Miguel (1954). Most workers find that different batches of cephalin-cholesterol reagent differ greatly in sensitivity (Maizels 1946, Endozien 1958) and are sensitive to light (Neefe and Reinhold 1944), and that the test, though giving abnormal results in many cases of liver disease, offers little help in discriminating between hepatitis (80–100% positive) and other diseases whether of the liver (0–96% positive) or not (0–64% positive). These figures are from Hanger (1939), Pohle and Stewart (1941), Mateer et al. (1947), and Neefe et al. (1947). This test depends mainly on the total globulin of the serum.

The former tests depend on the interaction of serum with a preformed colloid; but there are tests which first produce a lyophobe colloid from serum and then flocculate it. All these depend on the breakdown of the lipoprotein complex by a phenol (Maclagan 1944a, Kunkel and Hoagland 1947), the liberated lipoid forming a colloidal solution which is flocculated by serum-proteins just as a preformed colloid would be. The flocculate contains lipoid, β- and γ-globulins (Maclagan 1944b, Cohen and Thompson 1947). The first of these tests was Vernes' (1929) resorcinol reaction, in which serum was diluted with an equal volume of 1·25% resorcinol in distilled water; Vernes regarded this reaction as a good index of tuberculous infection if it were found repeatedly positive; the precipitate consists mainly of fast-running γ-globulins, with a trace of albumin and β-globulin; it contains some lipoid. The best known is Maclagan's (1944b) thymol turbidity test, using a barbitone buffer of pH 7·8, ionic strength 0·01 saturated with thymol, while Kunkel et al. (1948) attempted to make the reaction more specific for lipoid by using 1% phenol in 12% sodium chloride, thus preventing the precipitation of euglobulin. Unfortunately the specificity of the test is low, the correlation coefficient between turbidity and total lipoid being only 0·6. Phenols are, of course, not the only reagents which will separate lipoid from lipoprotein, for Macheboeuf (1928) and Macheboeuf and Tayeau (1929) showed that some soaps will do this, but with unusual restraint refrained from developing a test utilising this discovery.

The mechanism of the thymol test has been studied by its originator and by the same workers who have studied other flocculation reactions, and by Albertsen et al. (1950). The general conclusion has been that the thymol test is dependent on phospholipids and other lipids which decrease when nutrition is poor; and if lipids are present, is then dependent on γ- and β-globulin: there is also an inhibitor present in the serum of patients with obstructive jaundice, and this seems to be a muco-protein (Anderson et al. 1955, Maclagan 1957). Turbidity proceeds to flocculation when levels are high, and during the recovery phase flocculation ceases only when the albumin level has returned to normal. Recent work has questioned the significance of phospholipids, for Petersen has studied the phospholipid level in hepatitis (1953a) in which the thymol test is usually positive, and in obstructive jaundice, in which it is usually negative (1953b); in obstructive jaundice, increases in phospholipid are constant and large, persisting until the relief of obstruction, whereas in hepatitis the rise is less and brief, and in the most severe cases there was actually a fall. Russ et al. (1956) have also shown that in biliary cirrhosis the phospholipids are greatly raised though the thymol test is never strongly positive, though Gofman and Popper (see Pierce, Kimmel, and Burns 1954) find that in this disease the S_f 0–20 lipoproteins are enormously increased,

and Pierce, Kimmel, and Burns (1954) suggest that the thymol test depends on the whole range of lipoproteins from S_f 0 to S_f 100. It seems that components not usually found in serum such as the macro γ-globulin of Müller-Eberhard et al. (1956) may play a part.

Discussion

The significance of changes in the different components of serum has been discussed in an earlier paper (Discombe 1959). These flocculation tests are nowadays used chiefly in the differential diagnosis of liver disease, and there is no sense in multiplying tests which give the same information; in fact, Zieve and Hill (1955a–f) and Hill and Zieve (1957) have shown very clearly that if you do too many tests they so confuse the issue that you are less likely to come to a correct conclusion than if you depend on one or two carefully chosen tests. The tests of choice must be selected with the following intentions, *either*

(1) to estimate quantitatively some component of serum which varies considerably in disease, *or*
(2) to give maximum discrimination between two different pathological processes which have similar clinical manifestations.

Whichever intention is present, one should try also to select

(1) A test which is simple and can be done in the consulting room or ward side-room, but need not be very precise.
(2) A test which is precise, but which need not be particularly simple.

Of the tests available, one simple and one precise test for γ-globulin are useful; of the simple tests, Ray's hæmolytic test seems best, since all that is required is to dilute 1 volume of blood in 10 volumes of water, and inspect for a few minutes; while Kunkel's (1947) zinc-sulphate turbidity test is an excellent more precise measure of γ-globulin provided that carbon dioxide is excluded from the reaction mixture; it is the most easily quantified of the reactions. It seems doubtful whether very much useful information besides that obtained from the zinc-sulphate test is given by salting-out with ammonium sulphate, by adding non-ionic solvents, or by most of the heavy-metal tests.

The colloidal reagents are affected considerably by β-globulin and albumin as well as by γ-globulin, and can, therefore, give more information though in a form not easily quantified. The cephalin-cholesterol flocculation reagent cannot be standardised and the power of the test to discriminate between obstructive jaundice and hepatitis is not great—and it is uniformly positive in active malaria, just like its predecessor, Henry's melanoflocculation (Guttman et al. 1945). The colloidal-gold and colloidal-red tests are more reproducible, but even so are not remarkable for their discriminating power (Bauer 1937, Gray 1940, Neefe et al. 1947, Kallai and Keler-Bacoka 1957). Their chief advantage seems that they require no complicated apparatus; and it seems possible that alkali blue 6B, as suggested by Cabello and Miquel (1954), might prove to be the reagent of choice since it is available as a mixture of reasonably constant composition which can be prepared by dissolving a weighed amount of dye in distilled water.

The tests depending on dilution with a phenol are, however, quite different. The proteins do affect the thymol test, it is true, but there are hints that the active components of the globulins may be absent or present only in traces in normal serum; there is the inhibitory muco-protein, and above all, the lipoid component which must be present before the colloidal suspension can be formed. Diet plays a part, for badly nourished alcoholics often give negative thymol tests as outpatients when after admission and proper feeding for a week or two the test becomes strongly positive. The test is not particularly sensitive as an indicator of hepatitis, though it is positive in 86% or more of cases, but its discriminatory power between hepatitis and obstructive jaundice is great, for in the latter the test is either negative or only feebly positive even in the presence of severe illness. The test seems also to be of some value in following the physiological recovery of the patient, or the activity of the hepatitis, as Maizels (1946) suggested (Neefe 1946, Kunkel and Hoagland 1947, Maclagan 1947, Marner 1948, Kimmel et al. 1954). Not infrequently positive reactions persist for several months after the disappearance of jaundice, and during this time the patient often, but not always, feels tired and lacking in energy, recovering completely when the thymol has returned to normal. It is not difficult, however, to find patients who have progressed from acute hepatitis to terminal cirrhosis without making even a subjective recovery or acquiring a normal thymol test (Krarup and Roholm 1941). In relapses, the thymol often becomes more intense than in the initial attack and takes longer to return to normal.

The thymol flocculation test is even more delicate as an index of complete recovery. In my hands, once it has become positive it remains so until the serum-albumin has returned to normal; and Neefe (1946) noted that the two thymol tests were, together with the bromsulphalein test the best indices of activity and recovery. Both remain negative, however, in many mild cases of hepatitis and sometimes they do not become positive until a week or so after the onset of jaundice, while they are usually intensely positive in Hashimoto's disease and may be in Sjogren's syndrome.

The flocculation tests so far used offer useful help in differential diagnosis, but are in no way specific and give no help in differentiating between obstructive jaundice due to physical obstruction to the outflow of bile and that due to some non-anatomical abnormality which prevents outflow, nowadays usually termed cholangiolitic hepatitis in the early, and biliary cirrhosis in the late stages (Dible et al. 1947, Bjorneboe et al. 1952). In the late stage Russ et al. (1956) have found an enormous increase of lipoproteins with peptide/lipid ratios as low as 1 : 50, which readily dissociate, so that enormous turbidities can be obtained with the Kunkel phenol reagent or even by the simple process of freezing and thawing (see also Furman and Conrad 1957), even though the thymol test is normal or, at the most, slightly raised. Differentiation between the two forms of obstructive jaundice is important since "functional" obstruction seems to be rapidly overcome by corticoids; but this differentiation cannot as yet be accomplished by any battery of simple laboratory tests.

Use of Multiple Tests in Discrimination

In 1936 Sir Ronald Fisher, in a paper entitled The Use of Multiple Measurements in Taxonomic Problems, showed how to utilise most efficiently a few measurements so that individuals belonging to two similar species could be assigned to the correct species with the fewest errors and the least work. His methods have been applied to many other problems, including the selection of speciality salesmen; but for us it is only necessary to note that the taxonomic problem is logically identical with our problem of discriminating between the various sorts of liver disease, provided we are reasonably certain that

disease species other than those in our classification either do not exist or are very rare.

There are many difficulties in applying discriminatory tests of this type; first, of course, is the difficulty of defining the disease species which we will use, but even when this is overcome there are others—for example:

(1) Tests must be universally standardised (at present there are at least three sets of units for thymol turbidity).

(2) Results should be expressed in a numerical scale to facilitate arithmetic manipulation, though an all-or-none test could be scored.

(3) Tests must be neither too laborious nor too complicated for the ordinary hospital laboratory.

Thus, tests like colloidal red, shellac, benzoin, or cephalin cholesterol will be rejected because the reagent cannot be completely standardised and the results are not easily expressed numerically, while the estimation of urinary coproporphyrin would be frowned on because it has to be estimated either with a fluorimeter or a spectrophotometer and is not technically easy. Indeed, of the flocculation tests it seems that only the thymol turbidity and flocculation, zinc-sulphate turbidity, and colloidal gold or alkali blue 6B tests will prove to be sufficiently reproducible, and of these only the first three will be readily expressible on a numerical scale. Zieve and Hill (1955a–f) and Hill and Zieve (1957) have shown how proper choice of tests can minimise work and maximise useful information, and I believe their method of approach will have to be more generally adopted.

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RADIOLOGICAL DEMONSTRATION OF ENLARGED RETROPERITONEAL LYMPH-NODES

J. K. DAVIDSON
M.B. Edin., F.F.R.

SENIOR REGISTRAR (RADIODIAGNOSIS), ST. BARTHOLOMEW'S HOSPITAL, LONDON, E.C.1

C. W. H. HAVARD
B.M. Oxon., M.R.C.P.
MEDICAL REGISTRAR

R. BODLEY SCOTT
D.M. Oxon., F.R.C.P.
PHYSICIAN TO THE HOSPITAL

THE diagnosis and demonstration of enlarged retroperitoneal lymph-nodes not infrequently present a problem in clinical medicine. They are rarely palpable and the diagnosis of their presence must usually be made by inference. Blind irradiation of a large field is often the only therapeutic remedy.

We have, therefore, investigated the value of retroperitoneal pneumography as a means of escape from this diagnostic impasse. Twenty-two patients with Hodgkin's disease have been studied, and enlarged retroperitoneal lymph-nodes demonstrated in nine. There have been no complications. Confirmation of the radiological findings has been obtained in four cases at necropsy. The

technique is described and the nature of the radiological opacities and the limitations of the procedure are discussed.

Technique

The patient is prepared as for excretion pyelography. Preliminary radiographs are taken of the abdomen, including an anteroposterior tomogram, to ascertain the exact sections required following the insufflation.

The patient is then placed in the right lateral recumbent position with full hip flexion. After infiltration of the area with 2% lignocaine, a lumbar-puncture or Seldinger needle is inserted a little to one side of the midline and midway between the anus and coccyx. The needle is advanced in the sagittal plane, perforating the levator muscle. After 4-6 cm., the needle comes to lie in the relatively avascular tissue anterior to the sacrum and behind the rectum. During the insertion of the needle and the subsequent insufflation, the operator's finger is kept in the rectum, and the point of the needle is easily palpated deep to the rectal mucosa. 5–10 ml. of physiological saline is injected, and collects around the point of the needle. This fluid forms a pool through which the gas will flow, and is used in an endeavour to reduce the danger of gas embolism. Aspiration is attempted to ensure that the needle does not lie within a vessel.

The needle is connected to a two-way 50 ml. syringe through which filtered oxygen is run from a cylinder. 600 ml. of oxygen is insufflated slowly over 5–7 minutes; little pressure is required, and the examiner can feel the gas bubbling through the saline under his forefinger. Towards the end of the insufflation, the patient very often experiences a tight sensation in the left loin. The examiner then knows with certainty the gas is reaching the correct situation.

After 600 ml. has been insufflated, the patient lies on his other side and the procedure is repeated.

After insufflation of 110–1200 ml. of oxygen, the patient sits up and then walks about the room for 15–20 minutes. During this time, a tight " blown up " sensation is experienced in the upper abdomen, often worse on the right side. This lasts for a few minutes and eases off rapidly. In a few cases, it has been followed by a similar sensation in the chest and later in the neck: there have been no symptoms after 15–20 minutes. Percussion of the loins gives a tympanitic note, but this is of less value in localisation of the gas than the patients' subjective symptoms.

A radiograph is taken to see that the retroperitoneal structures are well outlined (fig. 1). A coned radiograph of the para-aortic area is then taken, centred on the second lumbar vertebra, and this is followed by anteroposterior tomography of the upper abdomen. The first tomogram is taken on the body of the first lumbar vertebra and subsequent tomograms are taken at 2 cm. intervals progressing anteriorly to cover the para-aortic area. Initially, right lateral recumbent tomograms of the same area were then taken at 2 cm. intervals, extending for 4 cm. on either side of the midline, and this was combined with the excretion pyelography to facilitate interpretation. Chest radiographs have been taken up to 3 hours after the insufflation and the presence of gas in the mediastinum has been demonstrated.

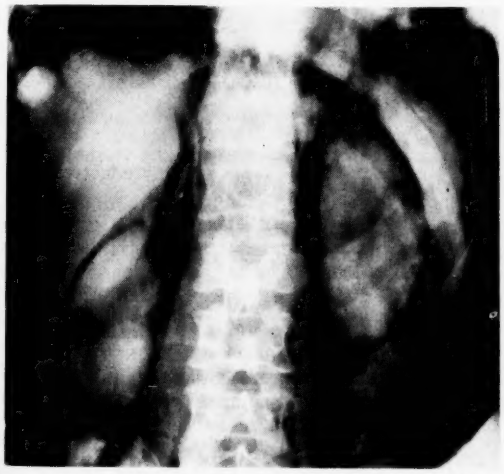

Fig. 1—Normal plain radiograph of the abdomen following presacral oxygen insufflation, showing good outlines of the liver, spleen, kidneys, psoas muscles, and diaphragmatic crura.

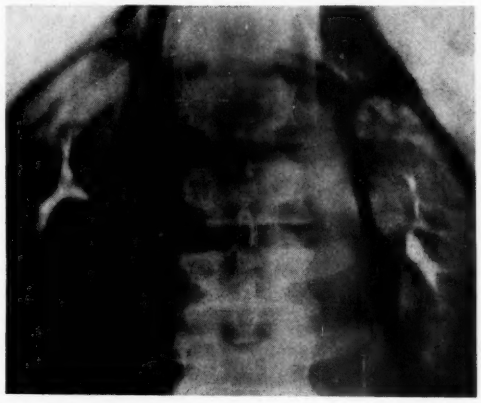

Fig. 2—Plain radiograph of the abdomen after presacral oxygen insufflation, showing the smooth dextra-convex opacity of the displaced inferior vena cava. Note in addition the enlarged nodes to the left of the midline.

Discussion

The introduction of air into the body as a means of contrast to tissue density has long been used in radiology. Carelli and Sordelli in 1921 introduced air into the renal fascia and achieved good outline of the kidneys and suprarenals. More recently, Ruis Rivas (1947, 1950) proposed the presacral route for the insufflation of retroperitoneal oxygen, and Blackwood (1951), Steinbach et al. (1952), and Lerman et al. (1953) established this procedure as a safe and useful diagnostic aid in the investigation of kidney and suprarenal disorders. Mosca (1951) describes 1500 presacral insufflations without any fatal complications. Russ et al. (1953) and Glassman et al. (1956) record non-fatal cases of gas embolism using the presacral route. However, gas emboli have occurred from this procedure. A recent nation-wide survey in America by Ransom et al. (1956) records 24 cases of fatal gas emboli by the presacral route in 9201 examinations, and 34 by the flank route in 221 examinations.

We feel that the possible risk of gas embolism is reduced by the use of a two-way syringe, which can carefully control the rate, the quantity and the pressure at which the oxygen is insufflated. Careful insertion of the needle into the relatively avascular area between the sacrum and the rectum, and repeated aspiration before insufflation, all tend to obviate this danger. The injection of saline is also an advantage. In the event of gas embolism, the work of Durant et al. (1947) establishes the left lateral recumbent position with the head lowered as the safest posture. Although the risk is reduced by using carbon dioxide, we have not found this satisfactory contrast medium, as it is too rapidly absorbed.

No complications have occurred in the thirty-eight patients we have investigated by this method.

The anterior skin surface of the abdomen receives a total of 5-6r from the anteroposterior radiograms.

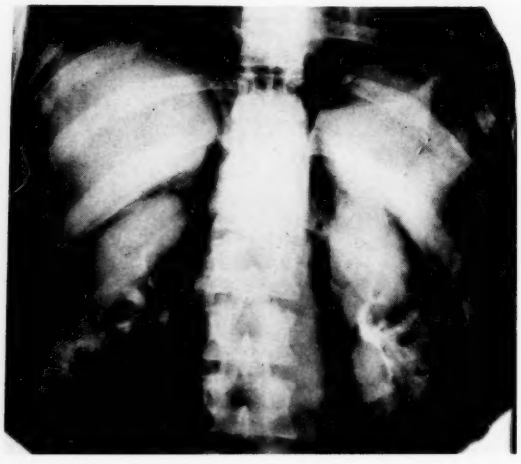

Fig. 3—Plain radiograph of the abdomen after presacral oxygen insufflation, showing left para-aortic opacity.

The French were the first to apply this method to the demonstration of enlarged retroperitoneal lymph-nodes in the reticuloses (Croizat et al. 1955). They followed the introduction of air by tomography in three planes. In the United States, Myerson and Wohl (1955) demonstrated enlarged lymph-nodes in four patients with reticuloses; their experience in attempting to localise metastases from testicular tumours suggested that this method would not adequately reveal lesions of less than 4 cm. in diameter.

We have found that the abnormality most frequently demonstrated is a smooth dextroconvex opacity extending over the right psoas muscle at the level of the upper three lumbar vertebrae. This has been interpreted as the result of displacement of inferior vena cava to the right by enlarged para-aortic nodes (fig. 2). This hypothesis is supported by the work of Helander and Lindblom (1956), who have demonstrated deformities in the inferior vena cava by expanding retroperitoneal lesions, using a technique of abdominal venography. This appearance may, or may not, be combined with an opacity extending to the left of the midline and overlying the left psoas muscle. This may be smooth, suggesting displacement of the abdominal aorta, or more lobulated; and has been tentatively interpreted as due to enlarged nodes (figs. 2 and 3). The opacities demonstrated in these radiographs were confirmed at necropsy as due to enlarged nodes. Occasionally the lobulated outline of enlarged nodes may be demonstrated to the right of the midline, in addition to the opacity of the displaced vena cava.

The radiographic appearances result from the displaced organs, or enlarged glands, being contrasted with the translucent retroperitoneal oxygen, in much the same way as mediastinal tumours are contrasted with the translucent lung fields.

Anteroposterior tomography confirms these radiographic appearances (fig. 4). Lateral tomography, however, is of limited value because of the difficulty in interpretation; furthermore, enlarged nodes are demonstrable only if their anterior borders are contrasted with gas in the stomach or other hollow viscus. Erect lateral radiographs, taken with the barium in the stomach, after retroperitoneal insufflation, make no further contribution.

The precise localisation of enlarged retroperitoneal lymph-nodes provides useful information for the management of patients with reticuloses. Wide-field irradiation is often undesirable in the face of a thrombocytopenia or lymphopenia: precise localisation of the disease may permit irradiation of a much smaller field. Another application of this procedure is in the differentiation of hepatomegaly or splenomegaly from enlarged lymph-nodes: this can, on occasions, be extremely difficult clinically.

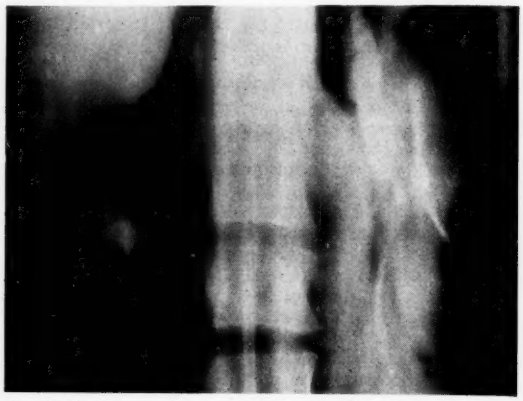

Fig. 4—Anteroposterior tomogram following presacral oxygen insufflation, showing enlarged para-aortic nodes to the left of the midline.

Summary

A radiological method of demonstrating enlarged retroperitoneal lymph-nodes is described. The practical applications and the limitation of the procedure are discussed.

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INITIATION OF VARICOSE VEINS
WITH OBSERVATIONS ON THE VESSELS AT THE PELVIC BRIM

T. HEATON WILLIAMS
M.B. Manc.

ASSISTANT LECTURER, ANATOMY DEPARTMENT, CARDIFF;
LATE ASSISTANT LECTURER IN ANATOMY, UNIVERSITY COLLEGE, DUBLIN

BEYOND the age of 45, about one in five women and one in fifteen men have varicose veins, and Gunnar Bauer (1950) has said that symptoms in the leg arise from chronic venous disease ten times as often as from arterial disease. In 1956 Dodd and Cockett concluded that the real cause of varicose veins is still unknown.

Some Hypotheses Reviewed

The true *initiating* cause of a disease has been defined as " something which, by coming into play, brings all the conditions into effective action and precipitates the effect " (Boyce Gibson 1930). *Contributory* causes may be important, but we have to try to distinguish between these and the initiating factor, which may vary from patient to patient.

1. *An Essential Weakness of the Vein Wall*

This seems to be a typical contributory cause which might be expected to affect veins anywhere—even as high up as the meninges where varices are sometimes found. Rogers (1939), Boyd (1948), and Anning (1956) regard an inherent weakness as important, and this might be inherited as a dominant defect. Eger and Wagner (1949) describe a defect of this kind in the saphenous sinus. Such a condition would be likely to weaken the defences for the assault of another factor.

2. *Hydrostatic Effect of a Long Column of Blood*

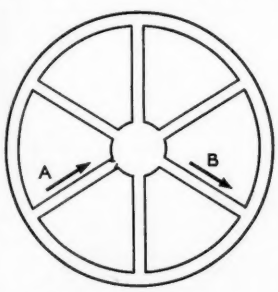
This has been blamed ever since men began to brood on the high incidence of varicose veins in those who stood for long periods or whose legs hung continuously from the saddle. Clearly, the fluid column will make a contribution towards establishing the condition, but if it were the major factor one would expect nearly all varices to start near the foot of the column and to be associated with incompetent iliac or femoral valves, which Basmajian's work (1952) disproves.

3. *Incompetent Valves in the Deep Veins*

Many authors believe that these play an important part in ætiology, and the incidence and distribution of these valves have often been analysed since Friedreich first investigated them in 1882. But what is the latest evidence? In 1952 Basmajian examined 76 paired male limbs: serious saphenous varices lay below excellent iliac valves, and there were no varices in those 20% of limbs which were without iliac valves. Similar results had been obtained by Hesse and Schaack (1911). Such findings throw doubt on the importance of this factor as well as on the influence of an uninterrupted column of blood above the saphenous valve.

4. *Incompetent Valves in Perforating Veins*

Dodd and Cockett (1956) are among workers who believe that destruction of valves in the perforating veins allows a reversal of flow along these vessels: the blood then leaks from the supported deep to the unsupported superficial veins, which are stretched beyond their elastic limit and so become varicose (see fig. 1). The evidence suggests that this does often happen; but by what mechanism are the valves in the perforators destroyed? What, in other words, is the true initiating cause?



A—Valves in perforator intact (blood flows from superficial to deep veins).
B—Valves in perforator destroyed (blood flows from deep to superficial veins).

Fig. 1.

5. *The Endocrine Factor and the Arteriovenous Anastomosis*

King of Melbourne (1950) has paired these two phenomena in a hæmodynamic explanation of the formation of the varix: he visualises two stages of development, early and late, and emphasises the need to study the condition in its early stage when the factors of causation are presumably active. At this time he finds the lesion localised, with the vein wall vascular, dilated, but very muscular, and he holds that in the early case the process is reversible. Quincke (1868) has ascribed the pulsation found in some veins to arteriovenous shunts, which had been described by Lealis Leal in 1707, and King believes that relaxation both of the arteriovenous anastomoses and the vein wall itself may be chemical in origin, probably hormonal.

Fried et al. (1953, 1956) have identified a condition which appears in early pregnancy and which, they think, has been confused with the classical saphenous varix. It differs in being sharply circumscribed, intradermal, often warm, tender, and tense, and usually causing pain severe enough to limit standing to a few minutes. They called it an "angiectic" and found that it responded to oral œstrogen or occasionally progesterone.

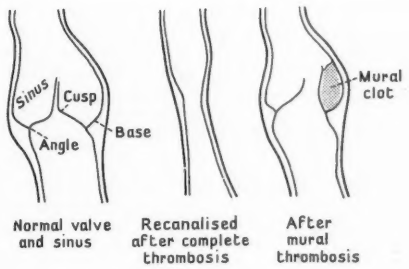


Fig. 2.

Here then are two possible ætiological links between hormones and varices; first King's arteriovenous shunts leading to veins with thickened vascular walls, which can become saccular later if the cause (probably hormonal) is not removed. Secondly, we have the cutaneous spider or angiectid which may be quite unrelated to the classical varicose vein. Do hormones and shunts occasionally or regularly participate in the formation of varicose veins?

6. *Thrombosis*

This may either destroy or damage venous valves, and it has been shown conclusively by Edwards and Edwards (1937) that complete thrombosis produces (after recanalisation) actually or functionally a valveless vein (see fig. 2). Incomplete or mural thrombosis produces changes comparable with the stenosis and insufficiency seen in heart valves. Although the cause of thrombosis has itself to be explained, we can see that this could produce varicose veins, either by destroying valves in the perforating veins, or by causing stenosis in the main veins draining the limb.

7. *Waves of Compression*

Adams (1939) presented the tempting hypothesis that intermittent compression by abdominal muscles in coughing and straining causes "waves of compression" down the veins of the lower limb. If the stress imposed on the vein wall exceeds its elastic limit, permanent dilation results and the valves become incompetent. However, varicose veins do not seem to have been linked statistically with excessive straining, and one can only surmise that this mechanism might account for some varices which start in the saphenous sinus.

8. *Chronic Venous Compression with Back-pressure Effects*

The importance of a chronic and maybe mounting back pressure is probably underestimated, and it is with this factor that I have been chiefly concerned. Cokkinis (1933) has mentioned the dragging effect of the loaded colon and suggested that it could account for the preponderance of left-sided varices. Turner (1939) described a slight degree of obstruction a little lower down—at the saphenous opening—and it is generally accepted that pressure on the iliac veins from a gravid uterus or tumour can bring about varicose veins.

In the loaded bowel or the gravid uterus we have true initiating causes, manifestly producing their effects by obstructing iliac veins. I think it likely that compression of iliac veins, brought about in a number of ways, may initiate varices more often than is generally believed.

Compression of Iliac Veins

The first question to be asked was whether the compression of the veins would seriously impede the return of blood from the limb.

Poiseuille's law, which relates the flow in a tube to the pressure, states that:

$$F = \frac{P \times \pi r^4}{8 \eta l}$$

where F is the flow in ml. per sec., l is the length considered and r the radius in cm., P is the pressure difference between

ends of the tube in dynes per sq. cm., and η the coefficient of viscosity measured in "poises". The resistance to flow has been derived by Burton (1952) from Poiseuille's law. It can be defined as the ratio of the driving force, the pressure difference, to the flow that results and is given by the equation:

$$R = \frac{8}{\pi} \times \eta \times \frac{l}{r^4}$$

Therefore

$$R \text{ is proportional to } \frac{1}{r^4}$$

or we can write:

$$R \propto \frac{1}{A^2}$$

where A is the cross-sectional area of the tube.

Although the formulæ above apply primarily to a cylinder, I have been able to satisfy myself at least that the last formula, $R \propto \frac{1}{A^2}$, could be applied to a large vein which is being compressed. If we use the formula in this way we see that if a cylindrical vein is flattened so that its

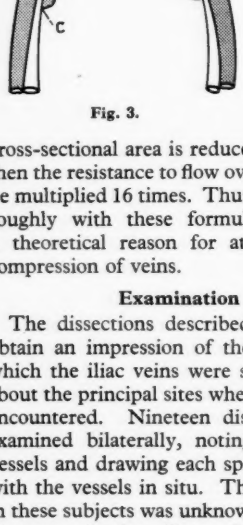


Fig. 3.

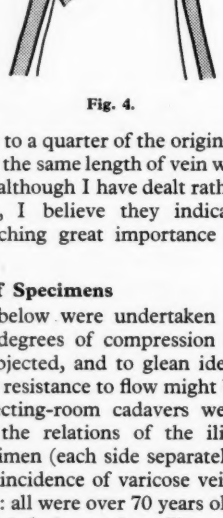


Fig. 4.

cross-sectional area is reduced to a quarter of the original, then the resistance to flow over the same length of vein will be multiplied 16 times. Thus, although I have dealt rather roughly with these formulæ, I believe they indicate a theoretical reason for attaching great importance to compression of veins.

Examination of Specimens

The dissections described below were undertaken to obtain an impression of the degrees of compression to which the iliac veins were subjected, and to glean ideas about the principal sites where resistance to flow might be encountered. Nineteen dissecting-room cadavers were examined bilaterally, noting the relations of the iliac vessels and drawing each specimen (each side separately) with the vessels in situ. The incidence of varicose veins in these subjects was unknown: all were over 70 years old. To ascertain the effects of embalming and senility two fresh postmortem specimens in the 3rd decade were also examined.

In all cases, young as well as old, there was good visible evidence that the iliac veins were constricted by arteries at the pelvic brim. The compression was greatest at three sites marked in fig. 3. The degree of compression in these positions showed great variation, but even in the fresh young cadavers compression was obvious at the most casual inspection.

In fig. 3, A indicates the end of the left common iliac vein where it is compressed by the bifurcating aorta or the origin of the right common iliac artery. Bearing in mind the formula for the resistance to flow, we appear to have an explanation for the preponderance of left-sided varices, in addition to the loaded colon of Cokkinis (1933).

B is a region over which the right common iliac vein often appears compressed as it lies behind the right common iliac artery. In one specimen in the 8th decade, in which compression seemed gross in this region, there was an anastomosis between the right internal iliac vein and the end of the right common iliac vein (fig. 4). In this subject varicose veins were present on the left side only.

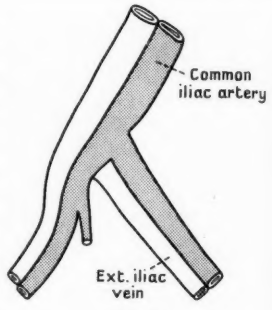


Fig. 5.

C marks the terminal part of the external iliac vein where it is crossed by the backward-plunging internal iliac artery. In some of the old subjects the artery appeared to embrace the vein here before passing back into the pelvis. Fig. 5 is a diagram of region C drawn from one of my series. Fig. 6 is a photograph of a dissected half-pelvis showing the commencement of the internal iliac artery hooking round the external iliac vein which I found to be quite tightly "squeezed" at this site. Even in the young subjects the flattening of the veins at C was conspicuous.

Discussion

The formula $R \propto \frac{1}{A^2}$, relating resistance to flow with the cross-sectional area of a tube, can be used to indicate that compression of a vein will seriously impede the venous return.

Bearing this in mind, the initiation of some varicose veins by compression of iliac veins by arteries seems to be a distinct probability.

Fig. 6.

Because the commencement of the inferior vena cava lies to the right of the bifurcating aorta, it follows that the artery-vein relationship will differ on the two sides below that level. This results in the veins being crossed at A and B. Compression at A often appears considerable and could well be responsible for the larger number of varices reported on the left (65 : 36, Cokkinis). I was interested to read the description, by Ehrich and Krumbhaar (1943), of an obstructive anomaly affecting the mouth of the left common iliac vein: they noted that the commonest site for this anomaly is *retroarterial*. Even without aneurysm or gross arteriosclerosis of the artery at A, pressure here is likely. Compression at C is also often considerable, and I have found no mention of this observation in the literature.

I have not been able to dissociate completely the effects of localised pressure, by arteries, from the more generalised pressure of viscera on the draining veins: in my opinion the two act together to obstruct, and thereby produce a back-pressure. A varicose vein will develop as soon as the total back-pressure overcomes the resistance of the elastic components of a vein wall in the limb below. Before this excessive internal pressure can act directly on the wall of an unsupported superficial vein, a valve in a communicating vein is put out of action. This mechanism of varix formation by compression of veins above the limb is only an extension of the special case where a pelvic tumour is responsible.

Several precedents exist for this hypothesis of compression by arteries. An aberrant renal artery running behind the ureter may be associated with hydronephrosis (Last 1954), and the clamping of the left renal vein between the aorta and superior mesenteric artery has been used to explain the overwhelming preponderance of left-sided varicoceles (Grant 1944). It may also be worth noting that one commonly finds a narrowing of the ureter as it crosses the arterial trunk at the pelvic brim.

If the mechanism I have described causes many varicose veins, it should be able to account for clinical and pathological phenomena associated with the disease. Verneuil (1955) in France first described a dilatation of the deep veins found together with the superficial varices. Is this not exactly what we should expect from a back-pressure which has gradually been building up until it is great enough to break down communicating valves? Back-pressure has been accepted as the cause of œsophageal "piles". This explanation would also account for the increase in incidence of varicose veins with age, the greater number in the left limb (see fig. 3A), the occurrence of varices in different parts of the limb (sometimes simultaneously), and the frequency of recurrence after local treatment. Compression of iliac veins could also bring about intimal adhesions and thrombosis.

If clinical investigation demonstrates the truth of the hypothesis, successful permanent treatment for varices initiated in this way will require, in addition to local therapy, the early separation of veins and arteries in the appropriate regions.

The apparent paradox of back-pressure without œdema has to be faced. It is known that the erect venous pressure at rest is about 90 mm. Hg (Pollack and Wood 1949), in contrast with figures of around 5–10 mm. Hg in the median basilic vein, in the cubital fossa. The rise in back-pressure which is sufficient to cause a blowout may be insufficient to disturb capillary pressure to the extent of causing a serious shift in fluid distribution. A compensating drop in the peripheral resistance by the opening of arteriovenous shunts in the limb would not improve the circulation in the skin capillaries, and a varicose ulcer might result.

Summary

The cause of varicose veins is still unknown. A distinction must be made between initiating and contributory factors.

The explanation put forward is that chronic obstruction and back-pressure are caused by compression of veins by iliac arteries. To act in this way the arteries need not be diseased.

Three common sites for such compression are described.

Pressure on veins by viscera, and local pressure by arteries at the pelvic brim, can act together, producing a total back-pressure which may become great enough to damage communicating valves. After that this back-pressure can act directly on the superficial vein walls.

This explanation is compatible with some of the more obvious features of the disease.

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"... I believe that of nationalism only cultures will remain—not the status but the dynamic aspects of cultures—their diversity, their creative powers, their profound sources of individual expression, languages, arts, concepts of good and evil, manners of expressing beauty and unravelling mysteries. ... The era of great regional unions is beginning. ... The furthering of regional unions is not a matter merely for politicians and economists. It is also a task for those who direct the institutions which are in the vanguard of thought. There has been no great event in history which was not first a spiritual reality."—The Hon. LUIS MUÑOZ MARIN, opening the Conference on Inter-American Exchange of Persons, Puerto Rico, Oct. 14, 1958.

CLEARING SYSTEM FOR BLOOD FATS
STIMULATION BY A HEPARINOID

CHARLES H. DUNCAN
M.D. Ohio State
ASSOCIATE PROFESSOR OF MEDICINE

MAURICE M. BEST
M.D. Louisville
ASSOCIATE PROFESSOR OF MEDICINE

CHARLES J. MCGAFF
M.D. Louisville
LATE RESIDENT IN MEDICINE

THE DEPARTMENT OF MEDICINE, UNIVERSITY OF LOUISVILLE, KENTUCKY

Hahn (1943) observed that injected heparin caused rapid clearing of the lipæmia following a fatty meal. Clearing of lipæmic plasma was also noted in vitro in the course of its incubation with plasma from a subject recently injected with heparin (Anderson and Fawcett 1950). Later studies have shown that, after heparin injection, lipæmia clears because of the presence in the plasma of an enzyme which hydrolyses the triglycerides of the chylomicrons (Robinson and French 1953, Shore et al. 1953). As the visible particles of triglyceride are hydrolysed the resultant fatty acids go into solution in association with plasma-albumin, and can be recovered quantitatively from the albumin fraction of the plasma-proteins (Robinson and French 1953). Although the clearing enzyme, lipoprotein lipase, has no direct effect on the cholesterol content of chylomicrons or lipoproteins, the cholesterol goes into solution in the course of clearing, presumably because of the fatty-acid protein complexes formed (Robinson et al. 1956).

Besides lysing of chylomicrons, lipoprotein lipase has been found to influence the concentrations of the various lipoproteins. Graham et al. (1951) noted that heparin caused a change in the ultracentrifugal distribution of serum-lipoproteins, there being a shift of the lipid from the high Sf classes to the lower classes. With separation of lipoproteins by paper-electrophoresis a similar effect of heparin was observed—namely, an increase in the proportion of lipid in the α fraction (Bolinger et al. 1954).

Heparinoids—i.e., anions of high molecular weight such as sulphonated polysaccharides or synthetic polymers—also produce plasma lipoprotein-lipase activity upon injection (Waldron and Friedman 1948, Brown et al. 1953). In this study such a heparinoid, polyethylene sulphonate (P.E.S.), has been given to a group of patients and its effect on clotting-time and on plasma lipoprotein-lipase activity compared with that of heparin. The effects on serum total-cholesterol and its partition between α and β lipoproteins of the sustained high lipoprotein-lipase activity produced by P.E.S. were studied also.

Methods

Coagulation-time.—Whole-blood coagulation-time was determined by a modified Lee-White technique employing four siliconised tubes and corks. Blood was collected with a siliconised needle and syringe, care being taken to avoid stasis or contamination with tissue fluids. The blood was kept at 37°C, the tubes being inverted and tapped lightly at 2-minute intervals to determine the presence of clotting. After the second tube clotted, the third and fourth tubes were watched, the coagulation-time being the mean time of clot formation in the last two tubes. Normal coagulation-time by this method is about 30 minutes.

Lipoprotein lipase.—Blood for in-vitro assay of lipoprotein-lipase activity was collected in citrated tubes packed in ice. After centrifugation at 2°C, the plasma was separated and kept packed in ice until the assay was performed (the same day).

A 1·2 ml. sample of plasma was placed in a 10×75 mm. cuvette, pre-warmed for 5 minutes in a 37°C water bath, and 0·4 ml. of a standard coconut-oil emulsion was added. The optical density at 500 mμ of the plasma and fat emulsion was read immediately in a Coleman Jr. spectrophotometer (against the plasma without fat emulsion as a blank) and again at the end of 30 minutes' incubation at 37°C.

Lipoprotein-lipase activity is expressed as the decrease in optical density (Δ E).

Serum-cholesterol.—Serum total-cholesterol was determined by the method of Abell at el. (1952).

α and β lipoproteins were separated by paper-electrophoresis, the strips were cut, and the cholesterol was eluted and determined as described by Langan et al. (1955). All separations and determinations were performed in duplicate, and the mean reported.

Comparison of Anticoagulant and Lipoprotein-lipase Stimulating Effects of Heparin and P.E.S.

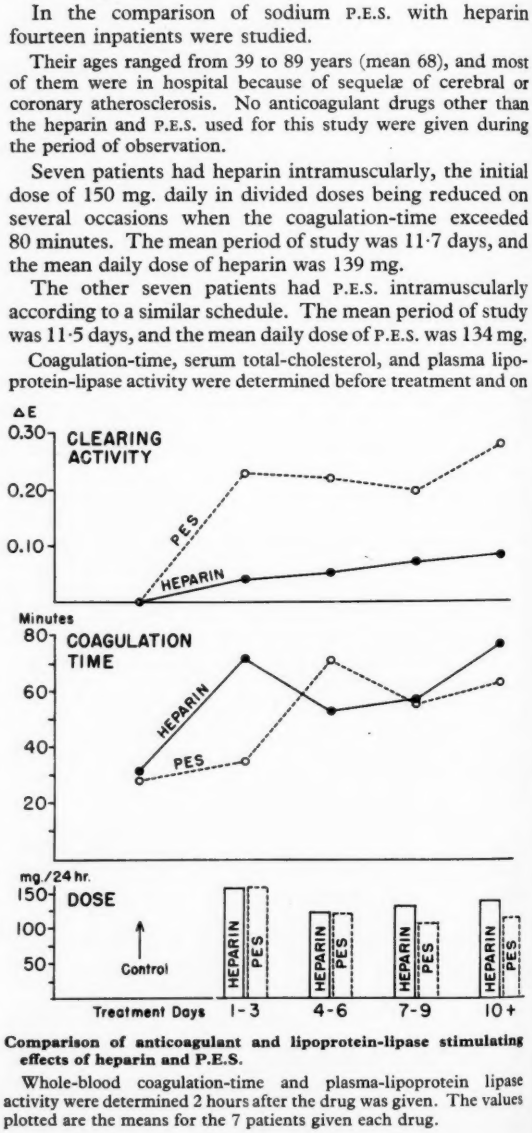
In the comparison of sodium P.E.S. with heparin fourteen inpatients were studied.

Their ages ranged from 39 to 89 years (mean 68), and most of them were in hospital because of sequelæ of cerebral or coronary atherosclerosis. No anticoagulant drugs other than the heparin and P.E.S. used for this study were given during the period of observation.

Seven patients had heparin intramuscularly, the initial dose of 150 mg. daily in divided doses being reduced on several occasions when the coagulation-time exceeded 80 minutes. The mean period of study was 11·7 days, and the mean daily dose of heparin was 139 mg.

The other seven patients had P.E.S. intramuscularly according to a similar schedule. The mean period of study was 11·5 days, and the mean daily dose of P.E.S. was 134 mg.

Coagulation-time, serum total-cholesterol, and plasma lipoprotein-lipase activity were determined before treatment and on



Comparison of anticoagulant and lipoprotein-lipase stimulating effects of heparin and P.E.S.

Whole-blood coagulation-time and plasma-lipoprotein lipase activity were determined 2 hours after the drug was given. The values plotted are the means for the 7 patients given each drug.

EFFECT OF P.E.S. ON PARTITION OF CHOLESTEROL BETWEEN α AND β LIPOPROTEINS

Case no.	Age	Sex	Diagnosis	Serum total-cholesterol and partition between α and β lipoprotein						Mean lipoprotein-lipase response* (ΔE)	Maximum increase in coagulation-time* (min.)
				Control			P.E.S.				
				Total (mg. per 100 ml.)	α (%)	β (%)	Total (mg. per 100 ml.)	α (%)	β (%)		
15	67	M	Diabetes mellitus, glomerulosclerosis, nephrotic syndrome	272	11·8	88·2	198	40·4	59·6	0·14	<10
16	55	F	Diabetes mellitus, myxœdema ..	340	20·0	80·0	216	43·5	56·5	0·18	48
17	55	M	Diabetes mellitus, hypertension ..	420	8·3	91·7	254	26·9	73·1	0·09	16
18	69	M	Cerebral artery thrombosis	314	14·5	85·5	295	31·7	68·3	0·09	29
19	51	M	Cerebral artery thrombosis	236	28·6	71·4	258	61·0	39·0	0·36	21
20	65	M	Chronic pulmonary fibrosis	213	13·8	86·2	199	30·8	69·2	0·14	<10

* 6 hours after P.E.S.

alternate days during the period of administration of heparin or P.E.S. Blood for these determinations was collected 2 hours after the drug was given.

The results are summarised in the figure. During the first 3 days, P.E.S. had less anticoagulant activity than did a similar dose of heparin. But, apparently because of a cumulative effect of P.E.S., the mean coagulation-times of the two groups were similar in the last week of the study.

A much more striking difference between P.E.S. and heparin was in their lipoprotein-lipase stimulating activity. P.E.S. had a mean clearing activity of ΔE 0·24 (S.D. 0·08), which is significantly greater ($P < 0·01$) than the mean clearing activity, ΔE 0·06 (S.D. 0·03), of a similar dose of heparin.

Changes in serum total-cholesterol were inconsistent. In the group given heparin, the mean control cholesterol was 251 mg. per 100 ml., and the mean treatment value was 250, the changes ranging from an increase of 23 mg. to a reduction of 16. In the group given P.E.S., the mean control serum-cholesterol was 290 mg. per 100 ml., and the mean treatment value was 272, the changes in individual patients ranging from an increase of 13 mg. to a decrease of 40.

Effect of P.E.S. on Partition of Cholesterol between α and β Lipoproteins

Because of the high levels of plasma lipoprotein-lipase activity on the patients who were given P.E.S., its effect on α and β lipoprotein cholesterol was studied, using six additional patients.

The major clinical features of these patients are given in the table. Control coagulation-time, serum total-cholesterol, and α and β lipoprotein cholesterol were determined on 2 consecutive days. Each patient was then given P.E.S. intramuscularly, 50 mg. 8-hourly for 8 days, except one (case 16) in whom the dose was reduced to 35 mg. from the 4th to the 8th days. Coagulation-time and lipoprotein-lipase activity of the plasma were determined every other day, the blood being collected 6 hours after P.E.S. was given. On the 7th and 8th days of treatment, the serum total-cholesterol was measured and the α and β lipoprotein cholesterol was determined in duplicate.

All the patients had significant plasma lipoprotein-lipase activity 6 hours after P.E.S., the mean ΔE being 0·16 compared to 0·24 in the first study when determinations were made 2 hours after the drug was given.

The first three patients, all diabetics with initially raised levels of serum-cholesterol, showed an appreciable fall in serum-cholesterol during the 8-day period of study. To what extent this was a result of the P.E.S. given and to what extent it was the result of improved regulation of the diabetes or other factors cannot be assessed. In the other three patients there was essentially no change in serum total-cholesterol. With regard to partition of cholesterol between α and β lipoprotein, however, the effect of P.E.S. was consistent. In all patients, regardless of whether total cholesterol changed, the percentage of the total cholesterol in the α-lipoprotein fraction was increased two to three times. Thus in the three patients whose total cholesterol decreased, the α fraction increased from a mean of 13·6% to 36·9%; in the three patients with unchanged total cholesterol the mean α fraction increased from 19·0% to 41·2%.

Discussion

There was no abnormal bleeding, alopecia, gastrointestinal disturbance, or other toxic or undesirable effect of P.E.S. during the short periods of these studies.

Although the variability of the individual coagulation-time responses to both heparin and P.E.S. makes comparison difficult, these studies suggest that a single dose of P.E.S. has appreciably less anticoagulant activity than heparin. This is in agreement with the observation of Kuo et al. (1958). When given for longer, however, P.E.S. appears to have a cumulative effect on coagulation, so that after several days P.E.S. and heparin have very similar anticoagulant activities. Dextran sulphate, another heparinoid, has also been observed to differ from heparin in that its anticoagulant effect is cumulative (Cohen and Tudhope 1956, Jeavons et al. 1956).

The effect of P.E.S. on serum total-cholesterol was equivocal. In the thirteen patients who had P.E.S. for 8 days or more, mean serum total-cholesterol decreased from an initial level of 294 mg. per 100 ml. to 256. But the decrease in the mean was largely due to the fall in cholesterol in three patients with diabetes mellitus, in whom factors other than the administration of P.E.S. may have been responsible. No dramatic hypocholesterolæmic effect was observed such as that reported from dextran sulphate (Cohen and Tudhope 1956, Jeavons et al. 1956).

In view of the evidence linking raised β-lipoprotein cholesterol levels with atherosclerosis, the effects of P.E.S. on plasma lipoprotein-lipase activity and on α and β lipoprotein cholesterol are of particular interest. Consistently higher levels of lipoprotein lipase were found in the plasma of patients given P.E.S. than in those given similar amounts of heparin. This finding seems to conflict with the report of Kuo et al. (1958), who observed similar clearing activity after single doses of heparin and P.E.S. A possible reason for this difference may be that in the

present study plasma-clearing activity was determined after repeated rather than single injections.

In any event, P.E.S. caused a consistent increase in the proportion of the serum total-cholesterol in the α-lipoprotein fraction. The extent to which the interval between injections of P.E.S. can be increased while retaining this shift of serum-cholesterol from β to α lipoprotein is being studied. If more prolonged administration of P.E.S. has no undesirable effects, it would offer a means of maintaining a sustained high level of lipoprotein-lipase activity. Such an agent would permit more definitive evaluation of the relationship of atherosclerosis to the distribution of serum-cholesterol between α and β lipoproteins.

Summary

The anticoagulant and lipæmia-clearing effects of a synthetic heparinoid, polyethylene sulphonate, have been studied. Compared with heparin, polyethylene sulphonate produced significantly higher plasma levels of lipoprotein-lipase activity. Its administration for an 8-day period resulted in the percentage of plasma total-cholesterol present in the α-lipoprotein fraction being increased two to three times.

We are grateful to the Upjohn Company, Kalamazoo, Michigan, for the heparin and the polyethylene sulphonate (U-6812) used in this study.

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CORRECTIVE ORTHOPÆDIC PROCEDURE IN A SEVERE HÆMOPHILIAC *

MARIO STEFANINI
M.D. Rome
DIRECTOR, JOSEPH STANTON MEMORIAL LABORATORIES; HEMATOLOGIST, SAINT ELIZABETH'S HOSPITAL, BOSTON, MASS.

THOMAS F. BRODERICK, Jr.
M.D. Tufts
CHIEF OF ORTHOPEDIC SURGERY, SAINT ELIZABETH'S HOSPITAL; INSTRUCTOR IN ORTHOPEDIC SURGERY, HARVARD MEDICAL SCHOOL AND TUFTS UNIVERSITY SCHOOL OF MEDICINE, BOSTON

FRANCO GOBBI
M.D. Pavia
FULBRIGHT SCHOLAR IN MEDICAL SCIENCES; RESEARCH FELLOW IN HEMATOLOGY, JOSEPH STANTON MEMORIAL LABORATORIES

MALVIN T. WHITE
M.D. Yale
CHIEF OF PLASTIC SURGERY, SAINT ELIZABETH'S HOSPITAL; ASSOCIATE CLINICAL PROFESSOR OF SURGERY, TUFTS UNIVERSITY SCHOOL OF MEDICINE

FEW if any elective orthopædic procedures have been carried out on patients with hæmophilia. DePalma and Cotler (1956) state that in their clinic two arthrodeses, two shelf-operations, and two derotation osteotomies for congenital dislocation of the hip have been performed; but they advise that such operations should be attempted only in patients with the milder forms of the disease. We here describe a major orthopædic procedure carried out on a severe hæmophiliac.

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The Case

History and Examination

An 8-year-old boy is the oldest of four brothers, all of whom are suffering from severe classical (type-A) hæmophilia (fig. 1). The bleeding tendency was discovered on the fifth day of life when attempted circumcision was followed by near-total exsanguination. Hæmorrhages since then have involved skin, various joints, and muscles with resulting slight limitation of movement of both elbows, wrists, and knees. There have also been epistaxes and episodes of hæmatemesis and melæna, especially during the spring and early fall. The patient has received over 250 transfusions of whole and fresh plasma.

Bleeding from a trivial injury at the age of 3 eventually resulted in severe right-sided equinovarus deformity. The patient walked awkwardly and slowly with a right short-leg antalgic limp. His right leg was thinner with 2 in. apparent and $^3/_4$ in. real shortening. He stood with his weight borne on the lateral malleolus and the projecting head of the talus (astragalus); the heel being in varus and the forefoot in 70° equinus and 60° varus (figs. 2 and 3). A thick bursa over the projecting head of the talus was discoloured from repeated hæmorrhages. The tendo Achillis, the posterior and anterior tibial tendons, the plantar fascia, and the toe flexors were contracted; and the muscular masses of the leg and thigh were wasted. Difficulty in walking resulted in frequent bleeding into both knee-joints and into the left ankle, threatening to cripple these articulations. We decided to operate to forestall this.

Investigations

The patient was admitted to hospital on Dec. 26, 1957. The hæmatological investigations gave the following results: hæmoglobin 14·1 g. per 100 ml., red-cell count 4,920,000 per c.mm., white-cell count 9100 per c.mm. (polymorphs 60%, eosinophils 2%, basophils 1%, lymphocytes 24%, monocytes 13%), platelets 251,000 per c.mm., hæmatocrit 46, and erythrocyte-sedimentation rate 15 mm. in one hour (Westergren). The tourniquet test was negative, the bleeding-time (Ivy) five minutes, and the clotting-time (in glass test-tubes), in several determinations, between two and six hours. Prothrombin activity was 100% in plasma and 98% in serum (after four hours' incubation). Thromboplastin generation was poor (fig. 4); and the poor prothrombin utilisation was corrected only by the addition of fresh plasma or of fresh oxalated plasma treated with $BaSO_4$. The activity of plasma anti-hæmophilic globulin (A.H.G.) was 2% and of the plasma thromboplastic component 98%. Fibrinogen was 375·2 mg. per 100 ml. There was no fibrinolysis by the test-tube or plate methods (Astrup and Müllertz 1952); and no anticoagulants or precipitins against A.H.G. were detected by standard techniques (Stefanini and Dameshek 1955). The response of the patient to plasma was tested before surgery (fig. 5). 1 unit (250 ml.) fresh plasma reduced the clotting-time of whole blood to twelve minutes, decreased serum-prothrombin activity to 15%, and raised A.H.G. activity to 50%.

The Operation

The management of the bleeding tendency before, during, and after operation is shown in fig. 6. Preoperatively a no. 20 polyethylene catheter was introduced into an antecubital vein to allow the continuous administration of blood, plasma, and drugs. The operation was carried out under 'Venethene' and open-mask ether anæsthesia: no tourniquet was used.

A sliding lengthening of the tendo Achillis gave an inch increase in length. The posterior tibial tendon was recessed to above the medial malleolus. The anterior tibial tendon was detached from its insertion at the base of the first metatarsal and cuneiform and drawn up into the midlateral leg through a second incision. An extensive plantar fasciotomy was then carried out, and the abductor hallucis was skived off the calcaneus. The head of the talus was next excised by sharp dissection, removing as little of the cartilage as possible. The

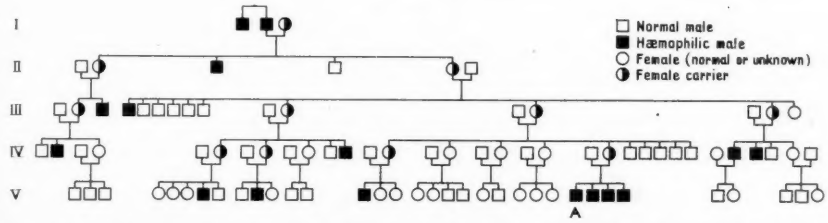


Fig. 1—Patient's family tree. Females are indicated as carriers only if they have borne hæmophilic children.

Information about generations I and II was obtained from generation IV, and some of it is probably incorrect. Information about generations III, IV, and V was checked by laboratory tests.

talonavicular (astragaloscaphoid) dislocation could then be reduced; and this made it possible to swing the forefoot into alignment with the hindfoot and to bring it up into almost neutral position. With the foot held in this corrected position a hole was drilled through the third cuneiform: the anterior tibial tendon was carried down from the lateral leg wound and anchored through this drill-hole, by means of a pull-out wire, to the sole and dorsum of the foot.

The result of the operation was a corrected foot, except for the flexion contracture of the toes which had become more evident with the decrease of the extreme varus deformity. The flexor hallucis longus and the flexor digitorum longus tendons were therefore divided subcutaneously at the lower crease of the metarsophalangeal joints. All wounds were closed with plain catgut in the deeper tissues and no. 000 ' Surgaloy ' wire to the skin. With the foot in relatively neutral position a padded long-leg plaster cast was applied.

The child had only two brief episodes of abnormal bleeding during the three and a half hours of the operation: on both occasions the plasma drip was interrupted briefly to inject packed red cells.

Postoperative Course

A spot of bright blood appeared on the cast within a few hours in the area corresponding to the amputated talus, but it did not spread. The patient received blood, plasma, and fluids through the indwelling catheter, which was left in place for fourteen days; when not used for other fluids, it was kept open with a slow drip of saline. The first cast was removed four days after the operation under thiopentone anæsthesia. The bleeding had been no different from what one would encounter in the usual triple arthrodesis: the six separate wounds about the foot and leg and the five tenotomy wounds all looked clean and healing nicely. Because the patient's condition appeared excellent, he received no blood or plasma during the twelfth and thirteenth postoperative days; but a spot of bright blood appeared on the cast on the morning of the fourteenth day. On removing the cast under thiopentone anæsthesia a small hæmatoma was found at the site of the plantar fasciotomy and where the head of the talus had been resected. The wounds were otherwise clean, and all stitches were removed. A cast was reapplied and transfusions were resumed. Three days later the patient started to walk. The cast was removed

Fig. 3—X-ray appearances before operation. Left: anteroposterior view. Right: lateral view.

without anæsthesia on Jan. 23, 1958, preliminary to discharge from the hospital: the hæmatoma at the talus site appeared smaller but that in the plantar area was larger, bulging, and fluctuating. To prevent pressure necrosis aspiration was attempted under local ether-chloride anæsthesia, but only about 1 ml. serous fluid could be withdrawn. Four of the six surgical wounds had healed entirely; the tendon transplant was functioning nicely; and the foot was in satisfactory weight-bearing position. The patient was discharged in a new, tight, short-leg cast with a walking-heel and asked to return every other day for transfusion of plasma. This he received on Jan. 25 and 27, but on Jan. 28 massive bleeding developed from the plantar area, blood flowing freely from the toe, opening. When the cast was removed, we found that the hæmatoma on the sole had ruptured: apparently the youngster had jumped off a couch, landing on the walking-heel and pushing it into the hæmatoma. The hæmorrhage was controlled by

(a)

(b)

(c)

Fig. 2—Preoperative condition of foot in (a) the dangling position, and (b) the sitting position. (c) Bursa over head of talus.

elevating the foot and by applying 'Gelfoam' and pressure bandage over the pulsating point. Despite fresh plasma or blood transfusions at regular intervals and despite tight pressure bandages, the bleeding twice recurred, though less severely. The skin sloughed on Feb. 13, exposing a crater about $1^1/_2$ in. across, filled with debris of gelfoam, gauze, and clotted blood. Even slight release of pressure was now followed by brisk bleeding; and it was felt that continuous pressure might eventually induce tissue necrosis. We therefore decided to operate.

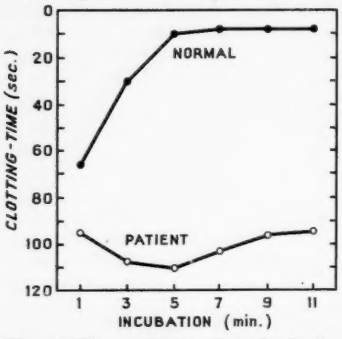


Fig. 4—The patient's thromboplastin generation compared with normal.

On Feb. 17 on removal of the dressing under general anæsthesia, a large clot was seen, covering an ulcer, about 2 in. across, on the arch of the foot. There was oozing from its margin, and from around the clot. On attempting to cleanse the wound, a jet of blood shot out and had to be controlled by strong digital pressure. The clot was then carefully removed, leaving the ulcer margins gaping widely. The plantar fascia appeared opaque, friable, and obviously necrotic; and from a small opening in it blood poured out under pressure. The necrotic fascia was removed and two large blood-vessels—probably the lateral plantar artery and vein—were revealed. The blood was issuing from a rent in the artery: the vein was intact but thin-walled. The vessels were dissected out and individually tied with no. 0000 wire both proximally and distally

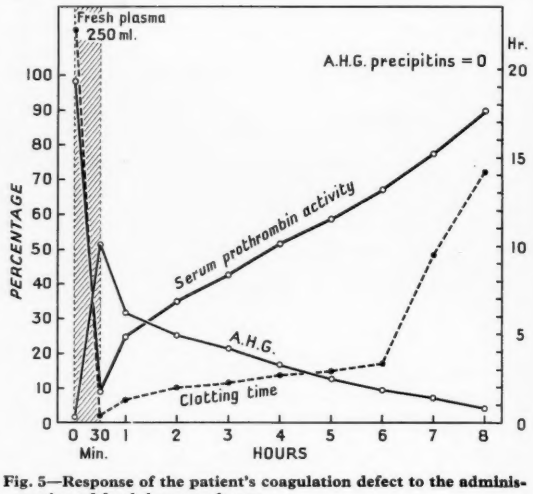


Fig. 5—Response of the patient's coagulation defect to the administration of fresh human plasma.

to the bleeding segment. 'Oxycel' was placed over the surface of the crater and a dry dressing under slight pressure over the entire operation area. A 'Kling' dressing was finally applied from the base of the toes to the upper calf. All dressings, except the oxycel, were changed four days later and thereafter every other day. 'Vaseline' gauze was applied to the wound after the oxycel was absorbed. Without further bleeding the wound began to fill from the bottom and three weeks later the skin closed. In April the patient was able to walk with crutches: in June he was walking with the help of a simple orthopædic shoe (to compensate for the $1^1/_4$ in. shortening)

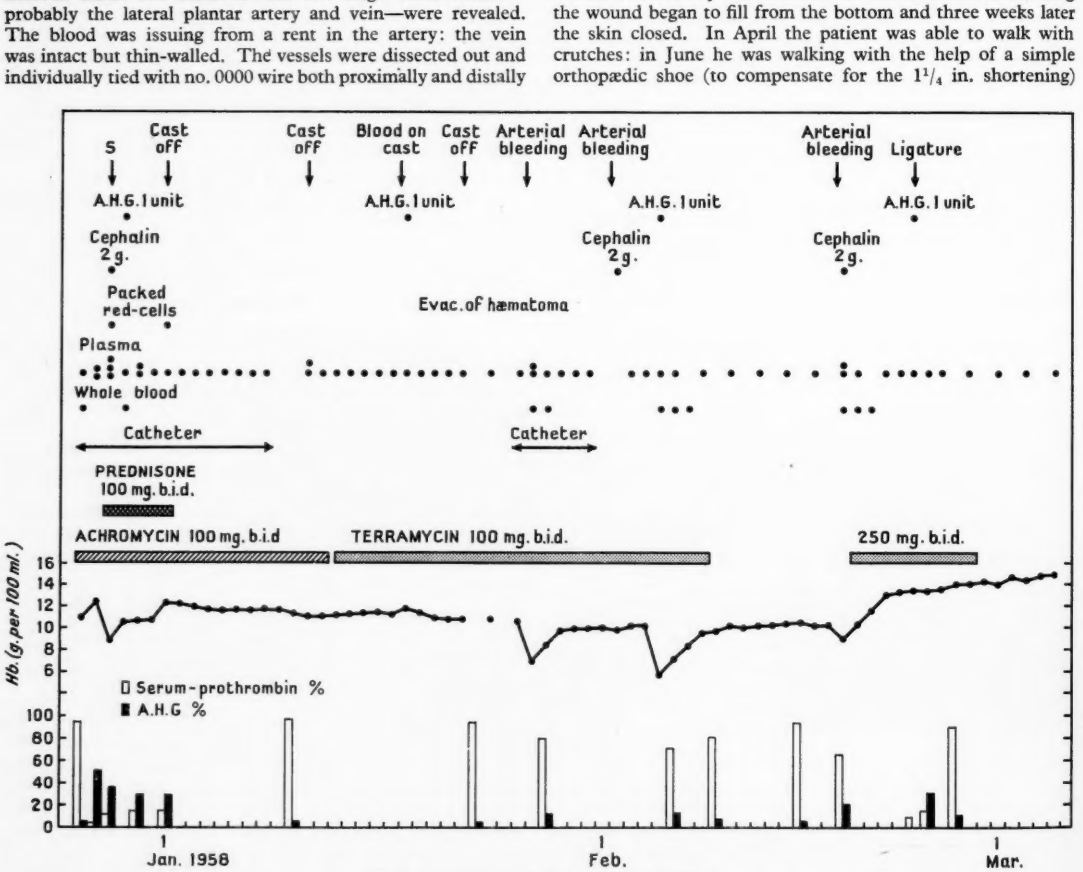
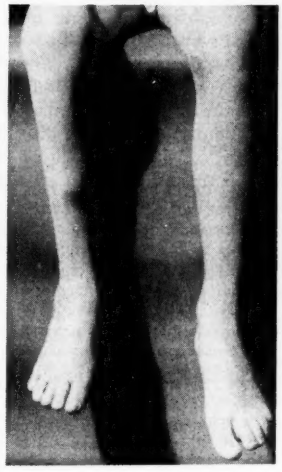


Fig. 6—Summary of the course of events.

(fig. 7). There has been no further bleeding into the ankle or knee joints and a physiotherapy programme has been started. The patient has continued of course, to have bouts of cutaneous hæmorrhages, and has recently suffered from an episode of severe gastrointestinal bleeding.

A year after operation the patient is normally active with an excellent gait. His thigh, calf, and foot have developed. The lateral transplant of the anterior tibial tendon functions strongly. Normal deambulation is achieved with a half-inch heel rise on the right shoe. X-rays best show the benefit achieved (fig. 8).



(a)

(b)

Fig. 7—Six months after surgery. Appearance of the limb in (a) the dangling position, and (b) the sitting position.

Discussion

Success in this case by no means invalidates the teaching that elective surgery in hæmophilia should be undertaken only in mild cases or under exceptional circumstances. Despite laboratory evidence that fresh frozen plasma, whole blood, or A.H.G. could correct the defective clotting mechanism only for a period of eight hours or so, injections at twenty-four-hour intervals proved adequate. No antibody developed, though, in the space of twenty days, the child received 10 pints of fresh blood, 2 units (500 ml.) packed cells, 60 units (15,000 ml.) fresh frozen plasma, 4 units concentrated A.H.G., and 3 units (2 g.) bovine cephalin; nor did 23 pints of saline solution give rise to electrolyte imbalance. All through his ordeal the child remained emotionally normal, though he became very dependent on doctors and nurses.

More cautious management might have prevented some of the complications. The original plantar hæmorrhage probably began when, after two weeks without bleeding, transfusions were discontinued for two days. In future we shall continue transfusions daily until closure of the skin is complete. The damage induced by the original hæmorrhage was aggravated when we attempted to preserve the vitality of the skin by removing the accumulated blood. The attempt was unsuccessful and may have been responsible for the injury to the plantar artery. This was the source of later bleeding; and the strong pressure that had to be applied before it was ligated threatened to destroy all that the operation had achieved.

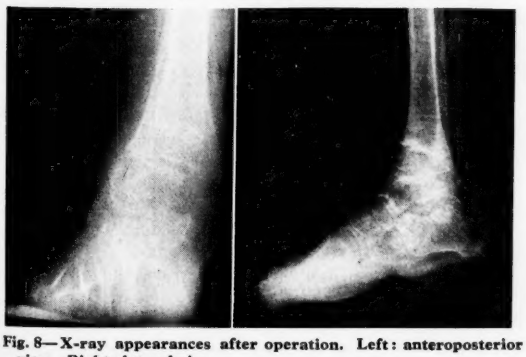


Fig. 8—X-ray appearances after operation. Left: anteroposterior view. Right: lateral view.

Summary

A complex elective orthopædic procedure—resection of the head of the talus, anterior tibial tendon transplant, multiple tenotomies, and fasciotomies—was carried out in an 8-year-old severe hæmophiliac.

The operation was ultimately successful; but the many difficulties encountered underline the need for careful planning and supervision.

An undertaking of this nature is not possible without the cooperation of many. We wish to express our appreciation to Dr. Burton Nault, assistant resident in surgery, for his assistance during the original intervention; to Dr. John Doherty, chief resident in surgery, who assisted during the last procedure; and to Dr. Samuel Gargano, resident in surgery, and Dr. Harrison Pearlson and Dr. Eugene Sweeney, interns, for very valuable help. Miss Frances Power, R.N., and Miss Kathleen Belliveau, R.N., of the blood-bank of Saint Elizabeth's Hospital, processed many pints of blood. The nurses of the pædiatric unit gave much competent assistance. Finally, the patient and ourselves are grateful to many volunteer donors from this city and from all parts of the country; and to the Blood Center, American Red Cross in Boston, for their generous cooperation.

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PENICILLIN-RESISTANT STAPHYLOCOCCI
INCIDENCE IN OUTPATIENTS WITH HAND INFECTIONS

A. J. BUHR *
B.A., M.D. Univ. Western Ontario
REGISTRAR RESEARCH ASSISTANT

J. C. SCOTT
M.A. Oxon., M.D., M.S. Toronto, F.R.C.S.

From The Accident Service, United Oxford Hospitals

ATTENTION is being focused on the rising incidence of penicillin-resistant strains of *Staphylococcus aureus* isolated from patients in hospital wards. Although this undoubtedly reflects a real increase in penicillin-resistant strains, it also represents the results of cross-infection while in hospital (Cairns and Summers 1950, Barber and Burston 1955), thus giving little information about the incidence of resistant strains in members of the general population. To obtain an indication of the latter figure for the Oxford area we studied strains isolated from hospital outpatients with hand infections. These were chosen because we had noted in this unit six years ago that of 82 *Staph. aureus* hand infections in which

* In receipt of a research grant from the Nuffield Provincial Hospitals Trust.

TABLE I—PROPORTION OF STRAINS OF *Staph. aureus* RESISTANT TO PENICILLIN AND CHLORTETRACYCLINE ISOLATED FROM 290 OUT-PATIENTS WITH HAND INFECTIONS

Group of patients	Total strains (no. of swabs)	No. of penicillin-resistant strains	% of penicillin-resistant strains	% of chlor-tetracycline-resistant strains
"General public" ..	271	81	30	6·2 (80 tested)
"Hospital staphylococcus contacts"	25	17	68	29·4 (17 tested)
Total	296	98	49	..

penicillin resistance was tested, no resistant strain was found (Scott and Jones 1952).

The strains investigated were coagulase-positive, and for our purposes were divided into sensitive and resistant categories according to their reaction on a penicillin gutter plate (Fleming 1942), containing 1 unit of penicillin per ml. of agar in the gutter. This reaction provides a clear division.

The methods of investigation and criteria were the same as those used by Cairns and Summers at this hospital in 1950, when they reported the incidence of penicillin-resistant staphylococci in relation to length of stay in hospital. The present study is a continuation of work in the same field.

Investigation

In 1957 *Staph. aureus* was obtained from 290 outpatients of our accident service who had 294 hand infections, from which 296 separate swabs were taken. 23 of these patients were doctors, nurses, physiotherapists,

TABLE II—RELATIONSHIP BETWEEN PENICILLIN THERAPY AND PROPORTION OF PENICILLIN-RESISTANT STRAINS OF *Staph. aureus* IN THE GENERAL PUBLIC

Therapy	Total strains (no. of swabs)	No. of penicillin-resistant strains	% of penicillin-resistant strains
No penicillin	187	50	27
Penicillin	84	31	37
Total	271	81	32

wardmaids, &c., and were classified as "hospital staphylococcus contacts".

There were therefore 267 members of the "general public" from whom 271 swabs were taken; of these 81 (30%) grew penicillin-resistant *Staph. aureus*. 80 of these penicillin-resistant strains were also tested for sensitivity to chlortetracycline; 5 (6%) were found to be resistant.

Of the 23 hospital staphylococcus contacts from whom 25 swabs were cultured, 17 (68%) grew penicillin-resistant staphylococci; 5 (29%) of these organisms were resistant also to chlortetracycline (table I). 3 organisms which were resistant to both penicillin and chlortetracycline were tested for resistance to erythromycin; all were sensitive to it.

An attempt was made to determine if there were any relation between penicillin therapy and the proportion of penicillin-resistant strains in the general public. Only penicillin therapy recorded for the hand infection under consideration was noted; previous penicillin therapy was not taken into account, mainly because detailed information was not always available. The findings are summarised in table II.

Further analysis showed no relation between the development of resistance to penicillin and the duration of penicillin therapy.

Only 4 hospital staphylococcus contacts had been given penicillin for the specific hand infection under consideration; 1 of these had been treated also with erythromycin. 5 swabs from this group of patients were sent for culture; 4 grew *Staph. aureus*, resistant to penicillin, but 3 of these were sensitive to chlortetracycline.

In order to provide a larger series of hospital contacts for comparison, we summarised the results of a separate review of all proven *Staph. aureus* hand infections in nurses treated here as outpatients between January, 1954, and April, 1958 (table III).

This suggests that the proportion of resistant strains is related to life in hospital rather than to penicillin therapy. 7 of these penicillin-resistant strains were tested for sensitivity to erythromycin; only 1 was resistant. The

TABLE III—RELATIONSHIP BETWEEN PENICILLIN THERAPY AND STRAINS OF *Staph. aureus* RESISTANT TO PENICILLIN AND CHLORTETRACYCLINE ISOLATED FROM 56 NURSES WITH HAND INFECTIONS

Therapy	Total strains (no. of swabs)	No. of penicillin-resistant strains	% of penicillin-resistant strains	% of chlor-tetracycline-resistant strains
No penicillin ..	36	32	89	..
Penicillin	22	19	86	..
Total	58	51	88	47 (51 tested)

figure summarises graphically some of our principal findings.

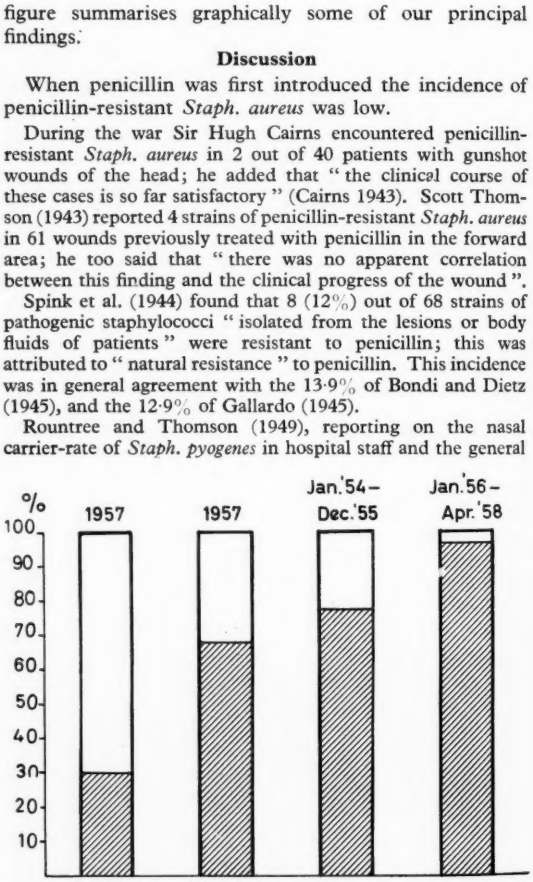
Discussion

When penicillin was first introduced the incidence of penicillin-resistant *Staph. aureus* was low.

During the war Sir Hugh Cairns encountered penicillin-resistant *Staph. aureus* in 2 out of 40 patients with gunshot wounds of the head; he added that "the clinical course of these cases is so far satisfactory" (Cairns 1943). Scott Thomson (1943) reported 4 strains of penicillin-resistant *Staph. aureus* in 61 wounds previously treated with penicillin in the forward area; he too said that "there was no apparent correlation between this finding and the clinical progress of the wound".

Spink et al. (1944) found that 8 (12%) out of 68 strains of pathogenic staphylococci "isolated from the lesions or body fluids of patients" were resistant to penicillin; this was attributed to "natural resistance" to penicillin. This incidence was in general agreement with the 13·9% of Bondi and Dietz (1945), and the 12·9% of Gallardo (1945).

Rountree and Thomson (1949), reporting on the nasal carrier-rate of *Staph. pyogenes* in hospital staff and the general



Penicillin-resistant and penicillin-sensitive *Staph. aureus* hand infections in outpatients.

population of Sydney, found that 32% of hospital staff were carriers of penicillin-resistant strains as compared with 4% in members of the community at large.

Meleney and Johnson (1953), reporting from the Presbyterian Hospital in New York on resistance to penicillin of coagulase-positive *Staph. aureus* recovered from infections treated in outpatients in their surgical service, noted that 17·8% were resistant in 1947–48, 29·1% in 1949, 43·5% in 1950, 43% in 1951, 31·1% in 1952, and 22·3% from Jan. 1 to May 1, 1953. They were concerned over the rising percentage of penicillin-resistant strains before 1951; they thought the falling off of resistant strains in later years was due to the widespread use of bacitracin and the combination of chlortetracycline ('Aureomycin'), oxytetracycline ('Terramycin'), and chloramphenicol ('Chloromycetin').

Serial reports from St. Bartholomew's Hospital by Griffiths et al. (1949), Birnstingl et al. (1952), and Rees et al. (1955) on penicillin-resistant *Staph. aureus* in outpatients from the casualty department with infections of the skin and subcutaneous tissues, recorded the gradually rising incidence of resistant strains—6·5% in 1949, 16% in 1952, and 21·5% in 1955.

Roodyn (1954), reporting on staphylococcal infections in general practice, found that of 93 strains of staphylococci from the pus of boils and styes 23% were penicillin resistant.

Fairbrother (1956) noted that the incidence of penicillin-resistant strains of *Staph. aureus* in outpatients with "infective processes" was 37% as compared with 33% isolated from material sent by general practitioners from a health centre.

Bolton et al. (1947) reviewed 100 pulp-space infections of the finger treated in the outpatient hand clinic of a general hospital; from 99 was grown a pure culture of *Staph. aureus*, coagulase-positive and penicillin-sensitive. This was in accord with the findings reported from our unit (Scott and Jones 1952), when, of 82 *Staph. aureus* hand infections in which penicillin resistance was tested, no resistant strain was found.

The rising incidence of penicillin-resistant *Staph. aureus* as a cause of hand infections in the Oxford area is reflected by the fact that, in 1957, this organism was cultured from 30% of 267 outpatients of the accident service with hand infections; this suggests a corresponding increase in the incidence of these resistant organisms in the general public.

Conclusions

The evidence suggests that there has been a disturbing increase in penicillin-resistant staphylococci both in the general population and in the hospital community, but especially in the latter group. Interest lies in the reasons for this, and in the measures to be taken to counteract the trend.

Our progress in medicine is not unlike the well-known game of snakes and ladders. The discoveries of Pasteur and their application to surgery by Lister, the evolution of "sterile technique", and the discovery of antibiotics provided us with ladders permitting revolutionary advances in the practice of surgery. The matter-of-fact acceptance of these aids, the failure to revise our own "hospital housekeeping", and, in particular, the misuse of antibiotics may quite easily bring us to worse conditions than those prevailing in the pre-antibiotic or even pre-Listerian era.

The following quotation from Meleney's paper (1942) on "Surgical Bacteriology" may well be apropos:

"On my return from France, I conferred with my friend and adviser, Dr. Whipple with regard to my further training in Surgery and he made this significant statement and prophecy —'In the past, surgeons have been anatomists. Now some of them are trying to be pathologists but the surgeons of the future will be physiologists, chemists or bacteriologists. Which do you want to be?' My interest in infection led me to choose bacteriology."

Summary

In 1952, in a report on hand infections from the Oxford accident service, it was found that, among 82 patients with *Staph. aureus* infections in which penicillin sensitivity was tested, there was no resistant strain.

In 1957 *Staph. aureus* resistant to penicillin was obtained from 81 (30%) of 267 outpatients with hand infections from the same unit. This group did not include "hospital staphylococcus contacts".

Of 187 outpatients from the general population who had not had penicillin for the hand infection under review, 27% grew penicillin-resistant strains of *Staph. aureus*, as compared to 37% of the patients who had had penicillin therapy.

Between January, 1954, and April, 1958, 56 nurses with proven *Staph. aureus* hand infections were treated as outpatients in the accident service; in this group 51 (88%) of the 58 strains of staphylococci were found to be resistant to penicillin. A further analysis of these findings showed that from January, 1956, until April, 1958, 30 out of 31 nurses (97%) with *Staph. aureus* hand infections had a penicillin-resistant staphylococcus.

With "hospital staphylococci" so often resistant to penicillin, all available methods should be used to reduce hospital infection. The introduction of antibiotics has increased the importance of all forms of aseptic and antiseptic precautions.

We wish to thank Dr. R. L. Vollum, bacteriologist to the United Oxford Hospitals, for help and advice in all stages of our work; Mr. Norman T. J. Bailey, reader in biometry, University of Oxford, for advice on some of the data; and Miss M. C. McLarty, our medical artist, for preparing the figure.

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TECHNIQUE FOR THE SEPARATE DIVERSION OF URINE AND FÆCES

R. T. TURNER WARWICK *
M.A., D.M., B.Sc. Oxon., F.R.C.S., M.R.C.P.
COMYNS BERKELEY RESEARCH FELLOW,
THE MIDDLESEX HOSPITAL, LONDON, W.1

AFTER pelvic exenteration or permanent destruction of both bladder and rectum, and occasionally because of tumours such as chordoma, it may be necessary to divert both urine and fæces. There are obvious disadvantages in a wet colostomy, in particular the management, but also the risk of renal infection if the ureter is dilated; several methods for separate diversion of urine and fæces have been devised. The procedure discussed here is simple

* Present address: The Francis Delafield Hospital and the Institute of Cancer Research, Columbia University College of Physicians and Surgeons, New York 32, U.S.A.

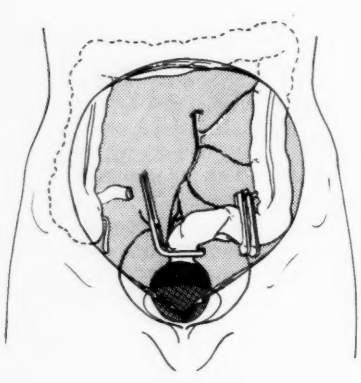


Fig. 1.

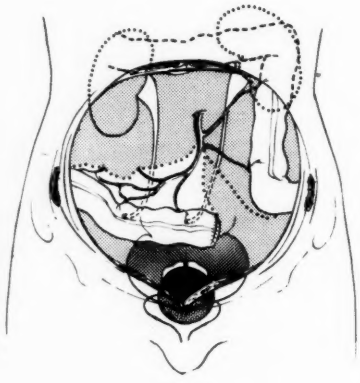


Fig. 2.

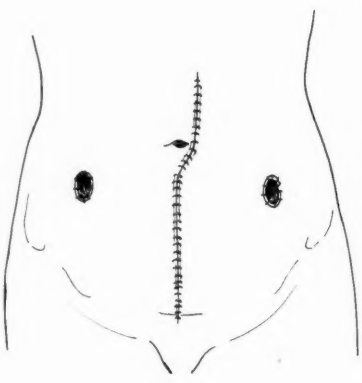


Fig. 3.

and not too time-consuming to be performed at the end of a radical operation.

The procedure is illustrated in figs. 1–3; but attention may be drawn to certain points:

1. For optimal fitting of the appliance, the surface sites of the colostomy and the ureterocolostomy conduit should be determined before operation.

2. To prevent pooling of urine in redundant loops, the isolated colonic segment should be as short as possible—not longer than 6–8 inches.

3. The pelvic colon is divided at a convenient site above the pelvirectal junction after ligation of the superior rectal vessels behind it. If the rectum is to be left in situ, its proximal end is closed and oversewn. If there is a rectal stricture, no excess

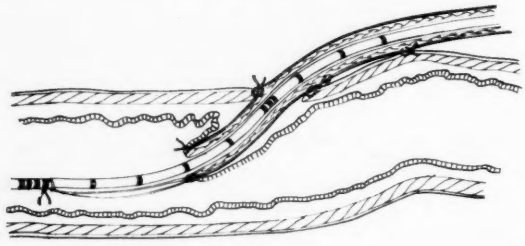


Fig. 4.

blind loop should remain above this, since downward passage of mucous secretions might be prevented.

4. The sigmoid colon is mobilised by gentle elevation of its mesocolon, and the distribution of the inferior mesenteric vessels is determined by transillumination (from a low-positioned spotlight). (Unless these vessels can be preserved this technique of diversion cannot, of course, be used.)

5. The colonic site of the colostomy is determined in relation to the length of the sigmoid colon, but essentially in relation to the distribution of the vessels. The mesocolon has to be deeply incised so that the isolated segment may be moved across to the right side of the abdomen on its vascular pedicle. If the vascular pattern does not readily permit the use of a good length of sigmoid colon for the colostomy, rather than make a long isolated loop it is better to divide the colon a few inches beyond the descending colon (on the basis of the lower left colic artery), and excise the excess sigmoid colon.

6. The colostomy is brought to the surface by the extraperitoneal route after undermining the lateral peritoneum.

7. It is often necessary to elongate the right side of the mesentery of the isolated segment, by division of a vessel at a suitably proximal site, so that the distal end of the conduit may reach the site of election (fig. 2).

8. A simple method of extraperitoneal exteriorisation of the right end of the segment is to mobilise the cæcum, and later allow it to overlie the lateral end of the conduit. This often facilitates the right ureteric anastomosis and reduces the length of the extraperitoneal tunnel to reach the site of election. At the conclusion of the operation the right half of the isolated colonic segment is therefore retroperitoneal, and the left half is sutured to the posterior parietal peritoneum so that it overlies the ureteric anastomoses. A similar procedure is used for isolated ileal conduits.

9. The ureters can be implanted into the posterior surface of the isolated conduit by the method of choice. Whether indwelling ureteric catheters are used as splints is a matter of personal preference, but it has the advantage of facilitating the anastomosis and of draining the urine direct to individual collecting-bottles during the first few days following operation. Thus immediate fitting of an appliance is usually unnecessary: a simple dressing absorbs the mucus and the small amount of urine which drains around the catheters.

10. A method of ureterocolic anastomosis which minimises ureteric reflux without tending to stenosis is illustrated in fig. 4. A semivalvular action is obtained by means of an intraluminal projection of the ureter which is protected by anastomosing its end to mobilised colonic mucosa, after which it is pulled well into the bowel and secured by seromuscular-adventitial sutures. If the ureter is anchored to the catheter to facilitate the pull-in, it is important to use a very fine (4×0) catgut suture through the extreme edge of the ureter so that the catheter can be pulled out at any time. A 2 cm. spacing-loop should be made in this anchoring stitch to allow the catheter to move without twisting the ureter.

This method of double diversion of urine and fæces can be used as a single-stage procedure in the presence of early urinary-tract obstruction, since dilated ureters can be implanted into the isolated bowel. If intestinal obstruction makes this necessary, colostomy can be performed as a first stage but the second stage is facilitated if the colostomy is sited with the foregoing principles in mind. Severe irradiation changes in ileum or colon may prevent their use for an isolated conduit.

No particular originality is claimed for this operation. It is merely a simple procedure for dealing with an unfortunate situation to the best advantage of the patient.

My thanks are due to my surgical chiefs, Sir Eric Riches and Mr. Cecil Murray. Mr. I. H. Griffiths has used a technique of ureterocolic anastomosis similar to that shown in fig. 4. The illustrations were drawn for me by Mr. Richard Neave.

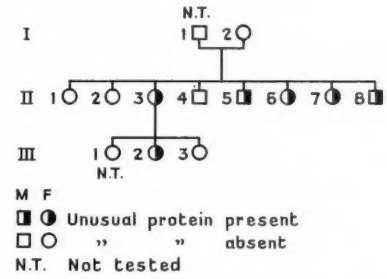
Preliminary Communications

A NEW GENETICALLY DETERMINED PLASMA-PROTEIN IN MAN

Smithies [1] has shown that electrophoresis in starch gel results in the resolution of a number of protein components in plasma which cannot be resolved in conventional electrophoretic systems. The particular fraction in conventional electrophoresis to which these newly identified components belong may be determined by a two-dimensional technique in which the plasma-proteins are first separated by paper electrophoresis and then resolved in the second dimension by starch-gel electrophoresis.[2]

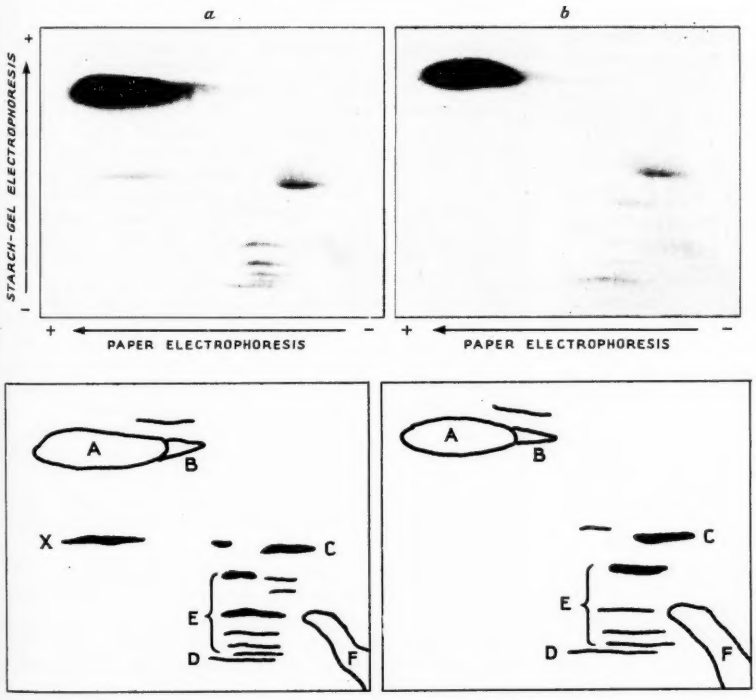
Using these methods we have recently encountered a number of individuals, all members of the same family, who possessed a plasma-protein component different in its electrophoretic properties from any of those usually observed in human plasma. The unusual protein could be detected by unidimensional starch-gel electrophoresis either in the borate buffer system described by Smithies,[1] in which it moved slightly faster than the fast α_2 component, or in the discontinuous buffer system (Tris/borate) described by Poulik,[3] in which it moved slightly faster than β-globulin C (transferrin). In such unidimensional systems the protein may however be confused with one of the inherited β-globulin (transferrin) variants recently described (Harris, Robson, and Siniscalco,[4] and Giblett, Hickman, and Smithies [5]). It was in fact most easily characterised in a two-dimensional system of the type described by Smithies and Poulik.[2] With this technique it was found that the unusual protein moved in the paper electrophoresis dimension with about the same mobility as serum-albumin. A comparison of such two-dimensional separations of the plasma-proteins from an individual with the unusual component and from one of his relatives without it shown in fig. 1.

1. Smithies, O. *Biochem. J.* 1955, **61**, 629.
2. Smithies, O., Poulik, M. D. *Nature, Lond.* 1956, **177**, 1033.
3. Poulik, M. D. *ibid.* 1957, **180**, 1477.



Pedigree no.	Sex	Date of birth	Date of death	Age at investigation (yr.)	Abnormal protein	Goitre + deafness	Haptoglobin type
I 1	M	1901	1948	..	n.t.	–	n.t.
2	F	1903	..	55	–	–	2-1
II 1	F	1924	..	34	–	+	2-1
2	F	1925	..	33	–	+	2-1
3	F	1926	..	32	+	+	1-1
4	M	1930	..	28	–	+	1-1
5	M	1931	..	27	+	–	2-1
6	F	1932	..	26	+	–	2-1
7	F	1934	..	24	+	–	2-1
8	M	1937	..	21	+	–	2-1
III 1	F	1951	..	..	n.t.	..	n.t.
2	F	1954	..	4	+	–	1-1
3	F	1956	..	2	–	–	1-1

Fig. 2—Pedigree of the family, and details of individuals shown in the pedigree.



KEY: A—albumin
B—α_1
C—β-globulin C (transferrin)
D—slow α_2
E—haptoglobin-hæmoglobin complexes
F—γ-globulin
X—unusual component

Fig. 1—A comparison of two-dimensional separations of the plasma-proteins from (*a*) an individual with the unusual component X, and (*b*) one of his relatives without it.

The paper electrophoresis dimension was carried out in an 0·05*M* barbitone buffer of pH 8·6, and the starch-gel electrophoresis dimension in the discontinuous buffer system of Poulik (1957). A small amount of hæmoglobin solution was added to saturate the haptoglobins.

The pedigree of the family in which the protein was observed is shown in fig. 2. The peculiarity is very uncommon, and its high familial concentration here strongly suggests that it is genetically determined. The individuals who possess the protein are probably heterozygous for a rare gene which is necessary for its synthesis.

The plasmas from members of this family were being examined

4. Harris, H., Robson, E. B., Siniscalco, M. *ibid.* 1958, **182**, 452.
5. Giblett, E. R., Hickman, C. G., Smithies, O. *ibid.* (in the press).

by starch-gel electrophoresis as part of a genetical linkage study of the syndrome of goitre associated with deafness [6] being carried out by one of us (G. R. F.) in collaboration with Dr. W. R. Trotter and Dr. M. E. Morgans. The family is no. 3 amongst those described by Fraser, Morgans, and Trotter.[7] Four members of the family (II 1, 2, 3, and 4) were goitrous and deaf, while the other members were not affected in this way. Since only one of the four individuals with the syndrome, and five out of the eight normal individuals studied in the family, showed the abnormal protein, its formation is evidently not specifically associated with the goitre-deafness abnormality. It also appears to be unassociated with either of the haptoglobin types segregating in the family.

Knedel [8] and Gitlin, Earle, Schmid, and Hutt [9] have described an inherited variant of serum-albumin. This occurred in about the same quantity as the normal serum-albumin present in the serum of individuals with the trait. It had an appreciably lower electrophoretic mobility at pH 8·6 than normal serum-albumin, and the two albumins could be readily separated from one another by paper electrophoresis. The new protein component reported here differs from this in that it was present in very much smaller quantities than the normal serum-albumin present in the plasma, and its electrophoretic mobility at pH 8·6 in paper was not obviously different from that of normal serum-albumin.

G. R. Fraser is the holder of a Medical Research Council scholarship.

Galton Laboratory, University College, London, W.C.1
G. R. FRASER B.A., M.B. Cantab.
Biochemistry Department, London Hospital Medical College, London, E.1
H. HARRIS M.A., M.D. Cantab.
Galton Laboratory
E. B. ROBSON PH.D. Lond.

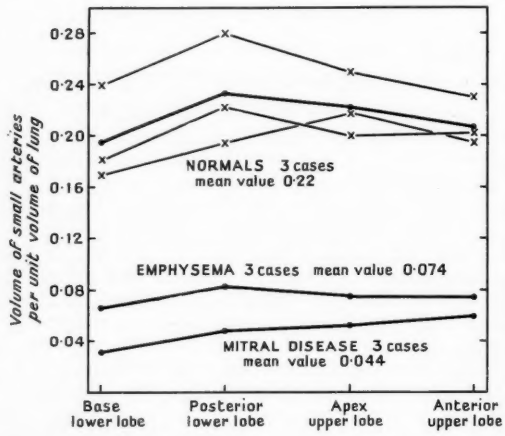
METHOD OF MEASURING THE VOLUME OF THE ARTERIAL BED IN THE PERIPHERAL PARTS OF CADAVERIC LUNGS

IN previous work we have encountered cases in which right heart stress detected clinically and confirmed at necropsy could not be explained by detectable disease in the rest of the heart or in the lungs. In particular in some cases diagnosed as chronic bronchitis and emphysema the right ventricular thickness was out of proportion to the apparent lung damage.

We concluded that measurement of the small-artery component of the vascular bed might be useful in accounting for these otherwise inexplicable instances of right heart enlargement.

METHOD

Much of the total volume of the pulmonary arterial bed is represented by the large branches of the main pulmonary artery. It has been shown that obstructive changes occur at the arteriolar level in cases of mitral stenosis, congenital heart-disease, and emphysema complicating massive pneumoconiosis.[10–12] Consequently we thought it important to measure the small-artery component, excluding parts of the lung containing large vessels. In the peripheral 2 cm. of the distended lung it is rare to find arteries exceeding 2 mm. in diameter. We therefore directed our study to the peripheral parts of the lung.



At necropsy the lung was carefully removed to avoid damage to the pleura. The hilar structures were then cut close to the heart so that as much of the main pulmonary artery as possible remained attached to the lung. The warmed lung was injected at 75 mm. Hg pressure with an injection fluid containing agar, propyliodone (' Dionosil ') and radioiodinated human serum albumin ^{131}I. The temperature of the lung and mixture was kept between 40°C and 45°C. The lung was then cooled and fully distended by injecting methylated spirit into the main bronchus. Radiographs were taken, the opaque propyliodone providing a qualitative assessment of the vascular bed.

Pieces approximately 40 c.cm. in volume were then cut from the periphery of the lung and the volumes of the pieces measured by displacement. The radioactivity in each piece was measured by placing it in the centre of a ring of six large Geiger counters.[13] The radioactivity was compared with that in a 10 ml. aliquot of the injection medium. We thus obtained the volume of injection mass in each piece of lung. For ease of comparison we expressed the result as the volume of injection mass per unit volume of distended lung.

Histological examination of the pieces showed that the injected material had entered the small arteries, but only occasional isolated small globules of it were found in the capillaries. The almost complete arrest of the injected material proximal to the capillaries was due to the presence of particulate propyliodone.

RESULTS

We accepted the amount of radioactivity per unit volume of lung as an index of the volume of the peripheral arterial bed. We have now used this method to study lungs from 34 cadavers. A few of the more interesting values are shown in the figure.

The results show a sharp quantitative difference between normals, those with mitral stenosis, and those with emphysema.

Our preliminary trials of this method lead us to think that it will be useful in helping to solve some problems in pulmonary hypertension.

We wish to thank Dr. Glyn Evans for facilities granted us at the Cardiff Radiotherapy Centre.

United Cardiff Hospitals
ARTHUR J. THOMAS M.D., B.SC. Wales, M.R.C.P.
Department of Pathology, Welsh National School of Medicine
W. R. L. JAMES M.D., B.SC. Wales
Cardiff Radiotherapy Centre
G. M. OWEN M.SC.

6. Morgans, M. E., Trotter, W. R. *Lancet*, 1958, i, 607.
7. Fraser, G. R., Morgans, M. E., Trotter, W. R. (in preparation).
8. Knedel, M. *Blut*, 1957, **3**, 129.
9. Gitlin, D., Earle, O. P., Schmid, K., Hutt, M. P. Fourth International Congress of Biochemistry, 1958. London.
10. Evans, W., Short, D. S. *Brit. Heart J.* 1957, **19**, 457.
11. Evans, W., Short, D. S. *ibid.* 1958, **20**, 529.
12. Wells, A. L. *J. Path. Bact.* 1954, **68**, 573.
13. Veal, N., Vetter, H. *Brit. J. Radiol.* 1952, **25**, 85.

Medical Societies

ASSOCIATION OF CLINICAL PATHOLOGISTS

THE Association's 62nd general meeting was held in Manchester on April 16–18. We publish below brief accounts of some of the papers presented at the meeting.

Hypofibrinogenæmia in Pregnancy

Dr. R. F. JENNISON had made a survey of the incidence of hypofibrinogenæmia in pregnancy. In 190 fibrinogen estimations in normal pregnancy, the mean fibrinogen level in the first trimester was 377 mg. per 100 ml., in the second trimester 443, and in the third trimester 487. The standard deviation was ±102 mg. per 100 ml., so that the 95% limits of fibrinogen levels were 283–691 mg. per 100 ml.; on this basis levels below 270 were considered to be pathological.

Of 117 patients with accidental hæmorrhage, 34 had a low fibrinogen, 15 below 150 mg. per 100 ml. 53 women in whom a dead fœtus had been retained in utero for longer than one week were also investigated and 13 instances of hypofibrinogenæmia demonstrated. In all these the fœtus had been dead for three weeks or more, and in 7 cases the fibrinogen level was below 150 mg. per 100 ml. Fibrinogen levels below 100 were also seen in abortion (2 cases), ruptured uterus (1), and possible amniotic-fluid embolism (2). There were no fatalities in this series. 24 of the patients with accidental hæmorrhage had blood or plasma transfusions, but only 3 of the cases of retained fœtus required treatment. Fibrinogen levels returned rapidly to normal after delivery irrespective of the type of treatment.

Effect of Heparin on Early Stages of Coagulation

Dr. J. R. O'BRIEN had found that heparin in critical dosage had no apparent effect on antihæmophilic globulin, factor V, factor VII, or platelet activity; the activation of coagulation by glass (Hageman factor) was not affected. There was evidence that heparin actually combined with an inactivated Christmas factor. The addition of protamine sulphate to such a heparin/Christmas-factor complex removed the heparin, thereby liberating Christmas-factor activity. Heparin could exist in two forms in plasma: "free" and available to delay clotting; or inactivated (presumably bound to some protein), and "unavailable" to delay clotting. The ability of coagulation factors to inactivate heparin had been investigated; the clotting-time of a thrombin-fibrinogen mixture was used to measure "available" heparin after the heparin had been added to the plasma fraction under study. Plasma-Christmas-factor, and especially serum-Christmas-factor, and platelet-protein (but not intact platelets) had been shown to inactivate heparin. The platelet-like activity of serum (P.L.A.S.) also inactivated heparin.[1] The ability of whole blood to inactivate heparin was determined during clotting, and the amount of heparin that could be inactivated increased notably soon after the blood started to clot; this was due presumably to platelet break-up, and to the formation of P.L.A.S. and serum-Christmas-factor. Critical quantities of heparin added to whole blood delayed clotting, probably owing to its effect on Christmas factor. Thrombin-generation and prothrombin-generation and prothrombin-consumption was normal, and no detectable heparin remained in the serum; presumably the heparin was inactivated before it could interfere with the intrinsic thrombin formed.

Exfoliative Gastric Cytology

Dr. A. I. SPRIGGS described the results of cytological examination for malignant cells in gastric washings from 155 patients. A simple saline-washing technique was used. Comparative cytological and histological examination was also made on a series of 24 freshly excised stomachs. Of 28 cases with carcinoma, malignant cells were identified in 55% in the first specimen. Dr. Spriggs recommended the use of sections of fixed sediment as a method which, although of relatively low sensitivity, was rapid and required no special training for technicians or pathologists. The examination of smears stained either by hæmatoxylin and mucicarmine, or with Papanicolaou stain, revealed malignant cells more often but was very laborious.

1. O'Brien, J. R. *Brit. J. Hæmatol.* 1955, **1**, 223.

Pulmonary Bone-marrow Embolism in Accident Reconstruction

Wing-Commander J. K. MASON described the study of tissue embolism in the lungs as a method for timing injuries. Fat embolism was unsatisfactory because of its frequency and the confusion surrounding its genesis. Bone-marrow embolism in the lungs, however, arose only after trauma to bone, and its incidence had been studied in 102 aircraft deaths associated with fracture. Emboli were found in 40% of such cases and were distributed at random in the lungs. If a minimum of five slides had been examined in every case, the incidence would have been about 60%. Emboli were uncommon when there was evidence of widespread instantaneous destruction of organs—in particular the cardiovascular system. Both fat and bone-marrow emboli arose with very great speed, the latter being found in 37% of deaths believed to be immediate. Both became more numerous with increased survival-time, but bone-marrow emboli resolved very much faster than fat emboli. An analysis of the two types of embolism could give valuable information about survival following injury, particularly after escape from aircraft by ejection.

Birth-injury to the Neck

In a random selection of 60 out of 213 deaths in the perinatal period Dr. P. O. YATES had made a histological examination for evidence of trauma to certain cervical structures. Only 2 babies, both breech deliveries, had shown much bruising of the spinal cord, but 9 subjects had nerve-root injuries and in nearly half the total there was damage to the spine with occasional tearing of ligaments and dura. The most surprising findings had been hæmatomas in the walls of the vertebral arteries in 24 cases which were often large enough to narrow the arterial lumen. They were thought to arise from tearing of the origins of arterial twigs supplying nerve-roots and spinal cord and could be of considerable importance, since ischæmic damage to the nuclei of the brain-stem would result in cardiorespiratory embarrassment and dysfunction of cranial nerves. Moreover, since the vertebral arteries were responsible for the blood-supply to the inner ear, the optic cortex, and part of the basal ganglia, those infants surviving moderate degrees of ischæmia might later show deafness, blindness, or one of the forms of cerebral palsy. The bilateral symmetry of some cerebral lesions in cerebral palsy, which had formerly been attributed to interruption of drainage into the great vein of Galen, could equally well be accounted for by stenosis of a vertebral artery.

Hand-drying

Dr. K. B. ROGERS emphasised that any hospital towel should be covered until it was used. Paper towels were disposable and relatively cheap but were rather rough on the hands, and very few dried the hands adequately if only one was used. Single cloth towels were too expensive to discard and the cost of laundering them was very high. Towels in long lengths were dry and æsthetically clean, but it was very difficult to use the piece of towel that had been most recently pulled off the unused roll; thus these towels were just as liable to be contaminated as any other. This had been demonstrated in the laboratory. None of the modern hot-air hand-dryers dried the hands fast enough for use in hospitals. Moreover, many of the present machines had their air inlet too near the floor, so that infected particles were liable to be sucked up from the floor and discharged into the air.

A cabinet had been designed which would provide a continuous warm, dry, and sterile towel. The cabinet contained boiling water, the steam from which would kill any non-sporing organisms on the surface of the towel. No damage was done to the cotton fibres of towels placed under tension and exposed to steam continuously for three weeks.

Serum-Isocitric-Dehydrogenase in Hepatocellular Damage

Dr. D. N. BARON and Dr. J. L. BELL had estimated serum-isocitric-dehydrogenase (I.C.D.) by the method of Wolfson and Williams-Ashman.[2] Their normal range was 2·5–9 units, and hepatocellular damage in infective hepatitis had raised this to as much as 900 units (in parallel with transaminases). A rise (20–60 units) followed the use of hepatotoxic drugs (e.g., iproniazid); and the level also increased in primary and metastatic hepatic malignant disease, and usually in cirrhosis. Serum-I.C.D. was consistently normal in posthepatic obstructive jaundice, and this might be valuable in differential diagnosis.

Serum-I.C.D. appeared more sensitive for the liver damage of clinical protein malnutrition than all other tests, including transaminases. In uncomplicated myocardial infarction, serum-I.C.D. was normal, but in heart-failure and liver enlargement moderate rises were found; in 1 case of prolonged hypotension, the serum-I.C.D. exceeded 200 units.

2. Wolfson, S. K., Williams-Ashman, H. C. *Proc. Soc. exp. Biol., N.Y.* 1957, **96**, 231.

Reviews of Books

The Rewards of Medicine

HUGH BARBER, F.R.C.P., physician emeritus, Derbyshire Royal Infirmary. London: H. K. Lewis. 1959. Pp. 140. 15*s*.

WHEN Sydenham was asked what book a doctor might most profitably read, he replied "*Don Quixote*". He may have chosen this work, having no obvious bearing on his profession, to point the lesson that the bedside, not the library, is the doctor's best place of study. Or perhaps he wished to commend Cervantes as an acute observer of human nature. Whatever the interpretation, Dr. Barber, for one, has taken the advice to heart, and he devotes a chapter of his new book to the lessons that can be learned from the adventures of the deluded knight.

Many of the other essays too reflect their writer's love of books, and his very wide acquaintance with them. One discusses the medical background of Jane Austen's novels, and another Smollett's criticisms of contemporary physicians. (Smollett, himself a doctor, had a number of influential friends, within and outside the profession. But did not Oliver Goldsmith, listed among the second group, also hold a medical degree?) This enjoyable book is written with a light touch that belies the author's admission that fifty-seven years have elapsed since his qualification.

Principles of Electrophoresis

RENÉ AUDUBERT and SERGE DE MENDE. Translated by A. J. POMERANS. London: Hutchinson Scientific & Technical Publications. 1959. Pp. 142. 30*s*.

THIS book by two distinguished French authors is excellently translated and is a welcome source of basic facts and technical details for the many workers now using electrophoresis. The late Prof. René Audubert taught both at the Sorbonne and at the Conservatoire National des Arts et Métiers; and the junior author specialises in electrophoresis at the National Centre for Scientific Research in Paris.

They discuss electrophoresis in conjunction with the general properties of electrolytes and colloidal systems, and they include a review of the moving-boundary method of Tiselius and the electrokinetic potential and determination of particle mobilities. There is also a useful review of electrophoresis in a supporting medium. The principles of paper electrophoresis are lucidly explained, and the role of evaporation and length of strip are clearly defined.

There are three practical chapters on the techniques of paper electrophoresis, on preparative electrophoresis in a supporting medium, and on future applications of electrophoresis, such as the analysis of isotopes with the determination of the half-life of radioactive particles. Each of the nine chapters is supported by well-chosen references.

Protection in Diagnostic Radiology

Editor: B. P. SONNENBLICK, PH.D., professor of biology, Newark College of Arts and Sciences, Rutgers University, Newark, New Jersey. New Brunswick: Rutgers University Press. 1959. Pp. 346. $7·50.

A READER who opens this book expecting to find a comprehensive textbook of protection in diagnostic radiology will be disappointed. Disappointment will turn to appreciation when he discovers instead a collection of reprints of 30 original papers on this subject spanning 17 years by authors from both sides of the Atlantic and from Australia. Many of the papers have been hard to obtain, and authors' reprints were often exhausted long ago. They discuss the protection of the X-ray worker and the patient, and consider some of the broader aspects of protection and ways of achieving it. The editor adds a comprehensive introduction and a short commentary on each of the 14 sections of the book. An extensive bibliography is appended.

This book is primarily a work of reference, and anyone responsible for radiation safety in hospitals, or for teaching radiation protection, will value it highly, though a certain amount of quarrying will probably be necessary to find any particular item, since there is no index.

Temporal Lobe Epilepsy

Editors: MAITLAND BALDWIN, PEARCE BAILEY. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1958. Pp. 581. £5 17*s*. 6*d*.

STUDY of the epilepsies has lately added more and more to our knowledge of the brain, for electrical techniques accompanying surgical exploration permit investigations on human subjects which are both necessary and experimental. The temporal lobe, a meeting-ground of psychiatric symptoms with organic damage, is of special interest. We lately discussed[1] some aspects of temporal-lobe disorder, and the great interest in the subject was reflected in two very busy international conferences—in Marseilles in 1954 and Bethesda, Maryland, in 1957. This book is the record of the second one. 38 authorities contributed, including almost all the leading figures in the field (from this country were E. Beck, J. B. Cavanagh, Murray Falconer, Denis Hill, A. Meyer, R. M. Norman, and John L. Wilson); and their papers and discussion are reported in full. The book is magnificently produced with detailed bibliography, charts, tables, and photographs. It will be the standard work of reference for some time to come.

Orthopædic Surgery (5th ed. London: Edward Arnold. 1959. Pp. 1075. 90*s*.).—The appearance of Sir Walter Mercer's textbook in a new edition is always an important event in the orthopædic world, where its status is comparable to that of *Gray* in anatomy or *Muir* in pathology. The book still wears its familiar binding, and its general format and chapter arrangement have been little altered. Several sections, however, have been completely rewritten (notably those dealing with scoliosis, bone tumours, and paralysis) and very many minor amendments have been made in others. Nicolas Andry's elegant little book, *Sur l'orthopédie*, destined to christen a new specialty, was published, not in 1757, but in 1741, the year before its author died. The later date has been repeated on the first page of text in successive editions of Mercer. The 1074 pages that follow continue to provide Andry's successors with one of the most instructive and authoritative guides to their subject yet written.

Lecture Notes on Pharmacology (5th ed. Oxford: Blackwell Scientific Publications. 1959. Pp. 144. 8*s*. 6*d*.).—In ten years Prof. J. H. Burn's small notebook of pharmacology has had five editions. It is up to date and authoritative and very useful for revision as an adjunct to lectures, though it is not quite full enough to be the student's sole textbook of pharmacology. Its popularity will continue.

1. *Lancet*, Feb. 28, 1959, p. 459.

THE LANCET

LONDON 16 MAY 1959

The Drug Bill

IN 1949 prescriptions issued under the National Health Service cost £30 million: in 1956 the figure was £57 million. To examine this increase and the reasons for it and to suggest ways to economy has been the task of two committees whose findings have lately appeared. The committee under Sir JAMES DOUGLAS was concerned with Scotland [1]; and Sir HENRY HINCHLIFFE was chairman of the committee which studied prescribing costs in England and Wales and whose report [2] is summarised on p. 1035. Both reports speak of waste; and whatever mitigations there may be in present circumstances of hospital and general practice, waste is a word that is hard to qualify or excuse. The Hinchliffe report seeks some solace in the fact that the rate of increase in the cost of the pharmaceutical service in recent years has been less than that in most other branches of the Health Service; but the real question is whether the drug bill itself can be justified. The report also sees one cause of a big drug bill in " the coincidental introduction of a free and comprehensive Health Service for all and the discovery and large-scale production of valuable but expensive drugs." But some of the expansion in drug manufacture was hardly " coincidental", for it was largely stimulated by the prospect of the National Health Service. And though new drugs have made a tremendous impact on tuberculosis and other infectious diseases, the return for large expenditure is elsewhere less substantial. As a measure of money well spent, what is needed, if it were possible, is an equation relating the rise in the drug bill on the one hand to changing mortality and morbidity on the other. Such precision may never be attainable, and justification for a rising drug bill may never therefore be fully convincing; but at least we can attack what looks like waste, and in that campaign the two reports can give valuable guidance.

" Better education " is now so ready a formula for all ills that it has become suspect; but we do not doubt that the committees are right in looking to changes in undergraduate and postgraduate education and in the supply of up-to-date information to doctors as the best way to reduce prescribing costs in the long run. Instruction in efficient prescribing is seldom a prominent feature of undergraduate education; and efficient prescribing will be, as the Douglas Committee declared, economical prescribing. At postgraduate level there is a distinct gap in the teaching of therapeutics, and we support the recommendation of more formal teaching for general practitioners and hospital staff. But who is equipped to give such instruction? The Hinchliffe report suggests that regional medical officers, of whom there are about 40 in England, could play a useful part in the postgraduate instruction of general practitioners; and in their interim report [3] the committee urged that greater use be made of regional medical officers in this way. Most of them, however, would need intensive coaching, even more determined, for instance, than that to which the medical representatives of drug houses are subjected; and they would have to expend much labour and enthusiasm to make their message effective.

The supply of expert and independent information about drugs to general practitioners must be augmented. The Douglas report recommends that *Prescribers' Notes* be issued more frequently, be made more topical, and include terse, candid, and independent evaluations of new drugs as soon as possible after they appear. The Hinchliffe Committee picture a *Prescribers' Journal*, an independent and authoritative publication to be distributed frequently to general practitioners, and to be run by a small council including physicians, general practitioners, pharmacists, a pharmacologist, and a statistician, with a whole-time editor. Another method of presentation, which the reports do not mention, is a desk-side card-index, on the pattern of the *Index of New Products* now issued by *The Pharmaceutical Journal*. The cards, like the proposed journal, would be prepared by an outstandingly well-informed and independent committee, aided perhaps by specialist panels. A full-time secretariat would also be needed. All new drugs and preparations would be scrutinised, and succinct notes about their nature, use, and cost recorded on a card for insertion in the doctor's own index. This innovation would be costly but it would, we think, be the one move that general practitioners would unreservedly welcome.

Prescription charges and other restrictive measures have seldom been popular with anybody. " The present prescription charge is a tax which, besides stimulating the wrong incentives, has proved disappointing financially." And, the Hinchliffe report adds, if any change in the basis of the prescription charge is contemplated it should not be introduced without an attempt to assess in advance its probable effects. Certainly there are now good reasons [4] to believe that the Treasury would have fared better if the Government had stuck to the old shilling-per-form system. In the matter of other kinds of restraint, the Douglas Committee, who are in favour of retaining charges but not increasing them, think that extravagance cannot be successfully confined by prohibitions on prescribing practice; and they go no further than to mention a possible trial in one or two executive-council areas of limitation of the quantity of drugs prescribable at any one time—a device which has substantially reduced the drug bill in New Zealand. The Hinchliffe Committee think it should be possible to reach an agreement whereby the amount of drugs supplied on one prescription would be limited either to that required for the patient's illness, if it is expected to last less than seven days, or to not more than a week's supply,

1. Report of the Scottish Committee on Prescribing Costs. H.M. Stationery Office, 1959. Pp. 48. 3*s*. See *Lancet*, May 2, 1959, pp. 926, 936.
2. Final Report of the Committee on Prescribing Costs. H.M. Stationery Office, 1959. 6*s*.
3. See *Lancet*, 1958, i, 1376.
4. Martin, J. P., Williams, S. *ibid*. Jan. 3, 1959, p. 36.

with exceptions for chronic or special cases. The committee advise the Minister to ask the professional bodies for their cooperation in determining the details of such a scheme, and they suggest a trial period of two years. If limitation of this kind proved successful, " it might be expedient to consider the abolition of the prescription charge "; and that would be welcome all round.

Both committees put high hopes on fuller cooperation with the drug manufacturing industry; but both reports contain passages which show an awareness that mere hopes of cooperation seldom save money. There are severe words, for instance, about inflated and expensive publicity campaigns, blunderbuss polypharmaceutical products (" the very antithesis of current teaching "), and claims for merit attributed to ingenious " blending " (" an ancient form of quackery assuming the guise of modern pseudo-science "). The Hinchliffe report points to three ways in which the prescriber can help to control costs: (*a*) by not prescribing expensive " elegant " products when simpler satisfactory preparations of the same drug are available; (*b*) by not prescribing unnecessarily elaborate polypharmaceutical preparations; and (*c*) by selecting the least expensive of the effective drugs available. The actions to be desired of the pharmaceutical industry, whose policy of research, production, advertising, and sales are primarily determined by the rules of commerce, are harder to define. The Hinchliffe Committee is enthusiastic about the voluntary scheme of price regulation: " it is a considerable step forward that the industry should recognise and accept the need for price regulation." So it is, and just over £400,000 a year is the estimated saving from price cuts already made; but can we hope for any big increase in this figure? It is significant that new preparations are exempt for their first three years. No true appraisal of the drug bill is possible until it is known just what proportion of the total turnover of a number of individual firms is absorbed in research, compared with the sums spent on sales promotion, advertising, and distribution. Doctors' letter-boxes daily proclaim that money is being spent lavishly on advertising in this branch of industry, as elsewhere; and both reports are keen to see cuts in extravagant overheads and selling campaigns. But it seems unlikely that any substantial reduction can be achieved in the present acutely competitive atmosphere, which encourages manufacturers to seize every opportunity to display their products in an expensive setting. It is hard to foresee agreement between manufacturers about advertisement expenditure, and such an " agreement " imposed by statute would be undesirable (and probably unworkable). There is more immediate hope of modifying the tone and claims of certain unjustified advertisements, and so reducing the likelihood of the products they extol being prescribed. Here the reports' suggestions about raising the standards of advertising do seem to need the support of a body to supervise and if possible enforce. The pharmaceutical industry would enhance its reputation if more of its members expressed open readiness to accept an agreed and universally enforceable plan for supervising advertisements.

An Oscillating Circuit

STUDY of the functions of the basal ganglia has acquired great impetus in the light of results of surgical intervention in cases of involuntary movements, sometimes called " hyperkinesia "—a word which has unfortunately been used also to describe an overall increase in normal movements of locomotion. The first successes in abolishing involuntary movements were obtained in parkinsonian tremor and rigidity. The early attempts stemmed from the observation that a patient with the parkinsonian syndrome in whom pyramidal disability subsequently developed from hemiparesis following a stroke might experience great improvement in the involuntary movements. Accordingly the first operations were directed at the pyramidal system—the cortex of areas 4 or 6,[1] the internal capsule,[2] the cerebral peduncle,[3] or the " pyramidal " tract in the spinal cord.[4] All were formidable operations in a debilitated subject, and all were accompanied by hemiparesis, of which the best that could be said was that it was not as great as might have been expected. A new era was introduced by the surgical attack on the globus pallidus,[5 6] pallidofugal fibres, [7–9] or nucleus ventralis lateralis thalami.[10] For the first time a substantial proportion of patients could be relieved of rigidity, and often also of tremor, without paying for their relief with paralysis. The early open operations were replaced by stereotaxic methods involving chemical or electrical destruction, and these are being practised increasingly often. A similar history applies to surgical endeavours directed at choreiform movements, including the violent hemichorea known as hemiballismus. These have culminated in a case reported by MARTIN and MCCAUL [11] in which the operation was directed at destruction of the nucleus ventralis lateralis of the thalamus on the side opposite to the hemiballismus. The result was complete relief of the involuntary movements with no greater signs of pyramidal involvement than increase in tendon reflexes on the affected side and slight abduction at the shoulder with partial flexion of the elbow when walking.

Obviously the time was ripe for a careful review of all that was known concerning the function and anatomy of the basal nuclei and related structures. This task was performed by Dr. PURDON MARTIN in lectures which are summarised in his article on the opening pages of this issue. Despite concentrated attention by many workers, the role of the basal nuclei in health remains singularly recondite. Experimental operations have proved unusually difficult to confirm by repetition—a feature possibly due to their depth and the complexity of the connections—and application of hypotheses from animals to human beings has often failed. Furthermore, observation of clinicopathological material has been

1. Bucy, P. C. *Res. Publ. Ass. nerv. ment. Dis.* 1942, **21**, 551
2. Browder, J. *Amer. J. Surg.* 1958, **75**, 264.
3. Walker, A. E. *J. nerv. ment. Dis.* 1952, **116**, 766.
4. Putnam, T. J. *Arch. Neurol. Psychiat.* 1940, **44**, 950.
5. Spiegel, E. A., Wycis, H. T. *ibid.* 1954, **71**, 598.
6. Cooper, I. S. The Neurosurgical Alleviation of Parkinsonism. Springfield, Ill., 1956.
7. Fénelon, F., Thiebaut, F. *Rev. neurol.* 1950, **83**, 280.
8. Meyers, R. *Res. Publ. Ass. nerv. ment. Dis.* 1942, **21**, 602.
9. Guiot, G., Brion, S. *Rev. neurol.* 1953, **89**, 578.
10. Hassler, R., Reichert, T. *Nervenarzt*, 1954, **25**, 441.
11. Martin, J. P., McCaul, I. R. *Brain*, 1959, **82**, 104.

fraught with the difficulty of interpreting the effects of diffuse lesions, fully observed only after death. PURDON MARTIN emphasises that in involuntary movements primary consideration must be given to structures that are *not* destroyed. He takes the view that the diseased parts do not function, because the symptoms are of a "positive" nature. This view is open to question: analogy with electronic circuits might lead the mind to different ways in which an "oscillating circuit" could be produced. In a smoothing circuit it is possible that no condenser is better than a faulty condenser, or an open circuit is preferable to a "dry connection". Lately MEYERS et al.[12] have reported that tremor is actually abolished by destruction aimed at the substantia nigra, which PURDON MARTIN regards as the structure "destroyed" in parkinsonism. The nuclei that PURDON MARTIN considers are the pallidum, the striatum, the subthalamic nuclei, and the substantia nigra. He concludes that damage to the subthalamic nucleus results in hemiballismus provided that the globus pallidus is intact. Similarly parkinsonian rigidity may be associated with degeneration of the substantia nigra, and evidence is accumulating that destruction of the globus pallidus or its efferent fibres will abolish such rigidity. Although the group of nuclei is concerned with muscular activity it is apparently not "immediately concerned with voluntary movement", for destruction of its efferent connections through the globus pallidus does not result in any defect of function that has been recognised. The system acts as a modulator—PURDON MARTIN believes that in health the subthalamic nucleus modulates impulses from the globus pallidus. Perhaps the analogy with a smoothing circuit is not after all too remote.

None of this evidence throws light on the function of the striatum, comprising the caudate nucleus and putamen. PURDON MARTIN concludes merely that its action is inhibitory or controlling. Experimental work has suggested that augmented forward progression may be produced by lesions of the head of the caudate nucleus, as well as by the premotor cortex.[13–17] Other experiments suggest that inhibitory effects mediated through the head of the caudate, and possibly also from frontal cortex, act on such "cortical automatisms" as grasping and biting.[18–20] From the results of experiments on rhesus monkeys, TURNER [21] suggested that augmented forward progression resulting from lesions of the head of the caudate nucleus were related to abolition of movements of recoil, or of arrest of forward progression. His results were marred, however, by concomitant damage to other structures, and have not yet been confirmed. No substantiated comparison of these findings in animals has been reported in man, in whom lesions in this region have not been accompanied by recognised increase in locomotor activity. Results of prefrontal leucotomy should furnish some cases of damage that has extended as far back as the head of the caudate nucleus, but no analysis of such cases from the locomotor point of view has come to notice.

If the key of one door to knowledge of the basal nuclei has been turned, the others remain obstinately locked.

12. Meyers, R., Fry, W. J., Fry, F. J., Dreyer, L. L., Schultz, D. F., Noyes, R. F. *J. Neurosurg.* 1959, **16**, 32.
13. Ruch, T. C., Shenkin, H. A. *J. Neurophysiol.* 1943, **6**, 349.
14. Mettler, F. A., Mettler, C. C. *Brain*, 1942, **65**, 242.
15. Mettler, F. A. *J. Neuropath.* 1945, **4**, 99.
16. Richter, C. P., Hines, M. *Brain*, 1938, **61**, 1.
17. Davis, G. D. D.Ph. Thesis, Yale, 1951.
18. Mettler, F. A., Ades, H. W., Lipman, E., Culler, E. A. *Arch. Neurol. Psychiat., Chicago*, 1939, **41**, 984.
19. Denny-Brown, D. *J. nerv. ment. Dis.* 1950, **112**, 1.
20. Denny-Brown, D., Botterell, E. H. *Res. Publ. Ass. nerv. ment. Dis.* 1948, **27**, 235.
21. Turner, E. *J. Neurol. Neurosurg. Psychiat.* 1957, **20**, 216.

"... will not take place"

THIS week we publish a long article in which Dr. GEIRINGER says that general practice in this country is still deteriorating. It will go on getting worse, he declares, until the National Health Service abandons the capitation system of payment and restores the "well-tried and logical method" of giving the practitioner a fee for each service rendered. In saying this he expresses, incisively, the opinion of quite a number of doctors in Britain and no doubt a large majority of those who criticise the N.H.S. from overseas. But in point of fact his main premise is no longer true. General practice *was* deteriorating, in this as in some other countries, and at first the N.H.S. accelerated instead of reversing the process; but in the past few years it has begun to recover. As for the financial tonic he recommends, we agree that monetary incentives should be used intelligently, in medicine as elsewhere; but we think that more harm than good would be done by changing to the method he proposes.

The capitation system is already under review: the Royal Commission may presently pronounce on it, and in due time the Porritt Committee will certainly do so. It has warm supporters, such as Lord TAYLOR, who called it "a great social invention", enabling "the State to pay the doctor for looking after his patients, without thereby giving the State the upper hand".[1] For our part, however, we incline to Sir FRANK NEWSAM'S [2] view that its long survival is due less to its positive merits than to its being less objectionable than the principal alternatives. The number of patients a doctor has is not an accurate index of the quality, or even the quantity, of his labour; and capitation is unquestionably one of the causes of the "'dumping syndrome', whereby anything looking like work is sent to hospital".[3] On the other hand, Dr. GEIRINGER is surely deluding himself when he says that a fee-for-service system "would automatically rehabilitate general practice, simply by the working of economic laws". He seems to have forgotten that in the old days the worst kind of "pauper medicine" was often given to the wives and children of panel patients—who paid (when they could) for each service rendered. The pursuit of fees has not always been pretty; nor is it always pretty today, even in prosperous communities where general practitioners have the all-round competence that Dr. GEIRINGER commends.

Simply to allow N.H.S. doctors to charge the Government a fee for each attendance on a patient would

1. Taylor, S. Good General Practice; p. 29. London, 1954.
2. Newsam, F. *Brit. med. J.* Jan. 17, 1959. Suppl., p. 12.
3. Paterson, J. K. *J. Coll. gen. Pract.* May, 1959, p. 160.

of course put an enormous premium on overdoctoring. So Dr. GEIRINGER proposes two safeguards: first, the patient would pay a contribution (say, half a crown), and secondly the N.H.S. payment to doctors would be made from a pool whose size was fixed in advance. "Any fee-for-service system would", he admits, "be a hotbed of abuses"; and on his plan we should ourselves expect increasing ill will among practitioners, who might suspect one another of performing unnecessary services and thus diminishing their colleagues' income. He believes that the inevitable drawbacks would be far outweighed by the advantage of allowing "good medicine to survive". Against this, however, we must point out that, though in some ways fee-for-service systems are admittedly preferable to capitation, they would still have very real defects even if they were not abused at all. Thus a medical committee examining the "schedule system" under which doctors in New Zealand are chiefly paid, said that its faults included:

(1) Failure to recognise that the practitioner's responsibility is to his patients, not to "complaints" or diseases. (2) Failure to encourage the educational and preventive aspects of family medical practice. (3) Failure to recognise the importance in the relationship between doctor and patient of certain human qualities which are functions of the medical calling at its highest. (4) Excessive emphasis on money values throughout.[4]

Two other possible schemes have lately come under discussion. Sir FRANK NEWSAM, in his report to the British Medical Association,[2] called attention to the "case system" devised by the late W. J. BRAITHWAITE and recommended to the Royal Commission on National Health Insurance in 1926. On this system the item of work, for which payments are made from the pool, is an *illness*—long or short—and the claim is established by the patient registering on first attendance.

"The advantages of this method", Sir FRANK said, "are chiefly psychological; the doctor would be glad to see the patient, at least on his first visit, and would take trouble over him, having an incentive to satisfy the patient and get him well. . . . It is the closest approximation to private medicine—indeed, it is akin to it, for in private practice most doctors find it impossible to have an exact system of fees but must modify them in many ways, so that their final bill ends up as a payment for the case. The incentive under this system is to become a true family doctor, to practise preventive measures and to give attention to other members of the family than the one who sent for the doctor. It is also a flexible system . . . Freedom of choice of doctor and patient is not 'natural' to the other systems but is ensured by this method."

In his instructive and constructive account of the fee-for-service system in New Zealand, Dr. A. W. S. THOMPSON [5] proposes a variant which is also based on BRAITHWAITE's idea. Under what he calls the "patient schedule system", doctors would be paid, out of a predetermined pool, according to the number of *separate patients* seen during the month, irrespective of the number of times they were seen. (The patient would himself pay a standard fee: "in New Zealand most of us are firmly convinced that a direct charge to the patient is an essential feature of a good scheme".) Though this suggestion has not yet been tried, it is based on Dr. THOMPSON's very large experience and deserves careful examination by the Porritt Committee. Nevertheless we shall be surprised if, after looking at all these other possibilities, British doctors are converted to any of them. Though we think that the capitation system needs to be made less crude, and that there is room for more kinds of supplementary fees providing incentives to useful work, we shall be surprised if capitation does not remain the basis of payment in the N.H.S. And we are not distressed by this, because, unlike Dr. GEIRINGER, we do not believe that a mere change in the method of paying doctors could be the salvation of general practice. Even under the present imperfect conditions, a great many doctors are doing very fine work indeed. To improve those conditions is important, but there was much truth in a remark by the late CHARLOTTE NAISH: "General practice has always been just what the individual practitioner wished to make of it".[6]

What, then, *ought* he to make of it (apart from an income)? So impressed were we, for many years, by the disuse atrophy of so many practitioners' skill, the narrowing of their work, and the corresponding decline in their status, that we repeatedly said some of the things Dr. GEIRINGER is saying so clearly now. Like him we have strongly deplored what he calls "the progressive hospitalisation of British medicine"; and, against those who saw no future for the general practitioner except as an appendage to the hospital service, we have insisted that, on the contrary, he must be brought back to his former position as a highly responsible doctor.[7] Other countries may have other patterns of medical care which satisfy them; but, with medicine dividing into more and more specialties, today less than ever do we see any preferable substitute for the continuing personal help of a doctor who feels responsible for his patient and is equal to that responsibility. Hence we cordially agreed with the main conclusion of the Collings report [8] that the conditions of practice must enable the practitioner to be (as we put it) "a real doctor, practising medicine in his own right, and not a superior orderly as some would have him".[9] At the same time we felt that COLLINGS (like GEIRINGER) was a little too much inclined to think in Australasian terms—wanting his ideal practitioner to be equipped and ready to deal with anything 500 miles from anywhere. In a small country like ours, with hospitals round every corner, the truly general practitioner—the man prepared to do anything in medicine or surgery—would now be a dangerous anachronism; and the British family doctor would clearly be wrong to tackle anything that requires a specialised team—except of course when he is acting as part of such a team. On the other hand, to suppose that, as a family doctor, he has no longer opportunity, and

4. Auckland Medical Practitioner Group. *N.Z. med. J.* 1952, **51**, 332; cited by Thompson (ref. 5).
5. Thompson, A. W. S. *Brit. med. J.* Feb. 14, 1959. Suppl., p. 51.
6. Naish, F. C. *Lancet*, 1952, ii, 484.
7. *ibid.* 1950, i, 548.
8. Collings, J. S. *ibid.* p. 555.
9. *ibid.* 1951, ii, 1071.

need, to practise real medicine is quite erroneous; and here Dr. GEIRINGER is giving an impression which is at most only partly accurate. In point of fact many doctors are now treating, in their surgeries and at home, a great many acute cases, from otitis media to pneumonia, which would formerly have gone to hospital; in cooperation with specialists they undertake the management of innumerable patients with such chronic diseases as he mentions (hypertension, diabetes, coronary-artery disease, and rheumatoid arthritis); and the very difficult care of the dying patients, for whom the hospital can do no more, is a heavy part of their responsibility. The statement, so often made, that general practice is nowadays concerned only with minor illness is simply not true.[10] By judicious use of consultations, which supply the specialised knowledge he must often lack, the family doctor can, as Dr. PATERSON [3] points out, remain a family doctor yet give his patients medical care of a high order.

When doctors, or other people, feel that their day's work brings a fair return, the exact way in which they are paid becomes less important; and, if technological advances bring real prosperity to this and other countries, our present interest in money will seem old-fashioned. That the condition and status of general practice depend on much besides techniques of payment is shown by the changes wrought in a few short years by the College of General Practitioners, which disclaims all interest in such matters. Already the college has amply fulfilled its promise to give leadership to general practitioners by general practitioners; and its influence, though multiform, is sufficiently evident from the statement in our news columns this week that some five hundred doctors lately attended one of its clinical meetings in Manchester. True, the advance of specialism, and other factors, had reduced general practice in this country to a precarious state: in the N.H.S. it has been too little regarded, and still it is often profoundly unsatisfactory, both for patient and doctor. But, though the form it will take in future has still to be worked out by trial and error, its Dark Ages seem to be ending in a very real Renaissance—not least because competition between practitioners is slowly turning into cooperation. Against the sometimes specious attractions of the specialties, its prestige is growing, and it has an increasing appeal to students, who see that at its best it offers them exactly what so many of them entered medicine in order to do. The family doctor of the future —perhaps as member of a group, perhaps as leader of a team, but certainly as the principal medical guardian of his patient—should be able to practise real medicine in circumstances less frustrating and more favourable than ever before; and one of the objects of the National Health Service should be to free him, once and for all, from his former inevitable preoccupation with money—whether his patients' or his own.

Looking at the present and the future rather than the past, we feel pretty confident that the murder Dr. GEIRINGER has announced will not take place.

10. *ibid.* Personal Papers. *ibid.* 1958, ii, 40.

Annotations

THE PERSONALITY OF THE EXPERIMENTER

DISCUSSING the use of psychology in relation to social factors, Prof. D. W. Harding wrote: " In a democracy, where the average among us tend eventually to get our way, the possibility of constantly developing our available fund of human resources demands techniques for helping those with special gifts to excel the rest of us." [1] There is surely no sphere worthier than that of research to receive any aid a psychologist can give, and so it was of particular interest to hear on May 6 and 7 at Bedford College, London, of the studies which Prof. D. J. van Lennep has been carrying out at the University of Utrecht.

Professor van Lennep suggested that research-workers fell into three basic categories. The " achiever " worked persistently and reliably on a problem set by management, using established methods and not requiring initiative and original thought. At the other extreme, the " creator " worked independently without terms of reference on problems of his own choosing for which no methodology existed. He put the past behind him and did not let it determine his thinking: older concepts existed only to be remoulded. Midway was the " problem-solver " who could bring to a solution a project which was clearly formulated but for which methodology was absent or inadequate. Taking three laboratories (two Dutch and one English), he obtained the supervisors' ratings of the workers on these three categories, and it appeared that the proportions and needs differed much between the three establishments. From a questionary a profile of the three groups emerged, although there was much overlap and clearly the ideal experimenter had the attributes of all categories. The achiever seemed to regard himself as ordinary, preferring a standard sort of life in the midst of a hierarchical system in which he saw his place. He thought his work useful to society and preferred regular step-by-step techniques. He did not think or worry about his work after hours and seemed to be at harmony with himself. The creator by contrast was rebellious: he did not wish for supervision nor care if his work was important to society. He was enthusiastic, talked about his results too soon, often omitting steps, and was apt to find that his discoveries had been made before. He thought he understood what a person was saying before the end of the sentence and felt a master of clock-time, fitting more into the day than he could cope with and working on several problems at once: his orientation was always towards the future. The problem-solver had much in common with the creator: he, too, strove for independence but felt that his results justified his existence. He did not omit steps, publish too soon, or repeat others' work in error. Being less occupied with the future he concentrated on and identified himself with present problems. Clearly the achiever was working creatively, although in a less pronounced way, and indeed he was often regarded as the most generally useful type of worker since a lively laboratory would have many more problems on hand than it could work on.

Devising further tests was difficult since the intelligence-quotient scale was generally regarded as stopping short of creativity: a new factor at a different, more " general ", level seemed to be needed; and such a test should be applicable to different disciplines. Professor van Lennep has employed aspects of the four-picture test

1. Harding, D. W. Social Psychology and Individual Values. London, 1953.

to study the matter further. In this test subjects are shown a slide with four unrelated pictures which they have to synthesise into a written story. Achievers were able to give a good coherent description, well-structured and grammatical, with a logical sequence of events, but it was an ordinary concrete communication taking in little outside the material presented. Problem solvers handled this matter as they handled problems, juggling with ideas and incorporating loose strains of personal imagination which, however, disturbed the original theme. The creator could take a central theme and develop the story from it, with anticipatory elaboration of future events. The striking feature was the ability to dispose of data in creating solutions with natural looseness and freedom. The 280 protocols were independently judged; the general validity of the test seemed to be statistically adequate, but the judges' reliability varied greatly. So great was this variation, indeed, that Professor van Lennep wondered how often the old argument of "clinical *v.* statistical" methods had foundered on people who were just bad clinical judges, irrespective of their degrees: he regarded judging the judges as an important subject for further work. His best judge showed 80% reliability on the presence or absence of the three types of ability compared with the views of laboratory management, and he suggested that the time is coming when such a technique with such a judge may be useful in selection.

Creativity, judged in this way, has been found by Professor van Lennep to be universal, and his test appeared to be equally revealing when applied to artists and even to those showing commercial creativity. In this work he has not used any current personality theory, deriving everything from observed facts; nor has he directed attention to the almost unexplorable "infralogical fringe" where ideas roam around the subconscious mind: Professor Kubie has well described the role which this "preconscious" region plays in creativity.[2] In closing, Professor van Lennep speculated on the nature of higher forms of creativity. In evolutionary terms he suggested that it might reflect greater and greater independence of the past such that a person was able to become "aware of awareness". Whereas the achiever relied on tradition and training, the creator became intellectually independent, seeing his past and "deconditioning" himself from it.

H.M. MEDICAL INSPECTORS

LAST week's white-paper[3] on the medical branch of the Factory Inspectorate should not pass unnoticed by the medical profession. Broadly, it approves a set-up which the medical inspectors of factories have often found unsatisfactory and irksome, and which we have criticised on various occasions. In a department which is primarily concerned with the health of industrial workers the doctors are permanently subordinate to members of other professions or to Civil Servants.

A previous survey of the staffing and organisation of the inspectorate was made by the under-secretary in charge of the safety, health, and welfare department of the Ministry, the director of organisation and establishments, and the Chief Inspector of Factories; and for this review of the medical branch the Senior Medical Inspector of Factories was added to their number. It is debatable whether a committee so constituted was able to take an impartial and imaginative view of the proper place of doctors in occupational health services; for instance, the Chief Inspector of Factories can hardly be regarded as an impartial adjudicator in an inquiry which touched his control of doctors and health. The white-paper, indeed, gives the impression that it could have been written without taking any evidence at all. Though the preface says that every member of the medical inspectorate was interviewed, and that written and oral representations from the Institution of Professional Civil Servants were received, their evidence is not given, and one cannot, therefore, judge whether it was given due weight. Where there is a hint of what was said by the doctors or the Institution, the proposal made is dismissed.

The report is divided into two parts, the first dealing with the duties and the second with the organisation and staffing of the medical inspectorate. The duties include visits to factories for various reasons, of which the one which is given priority is "to play their part in enforcement of the law"—which is surely not the primary function of a doctor. Another duty is "assisting in matters relating to the appointment of Appointed Factory Doctors, and maintaining contact with them in relation to their statutory duties." It is not mentioned that, for administrative purposes, the appointed factory doctors come under the lay superintending inspectors, a fact which the doctors commonly resent.

Still another duty is to undertake "planned" investigations of particular problems; but later it is stated that the medical inspectors are not to engage in research, which is to be done by the staff of the Medical Research Council. One can see the objections to turning the medical branch into a department for full-scale research; but the decision implies that the doctors best placed for research into problems of industrial health are not to be given the facilities to make the most of their opportunities. Possibly the main reason is that it would detract from their primary function of enforcement of the law.

It is conceded that medical inspectors should maintain contact with "medical and nursing personnel, e.g., Medical Officers of Health, Industrial Medical Officers and Works Nurses, medical staff at local [sic] hospitals and Universities". We strongly urged some years ago that the medical inspectors of factories should be attached part-time to hospitals, so that both the hospitals and the Factory Department and occupational health in general might benefit by closer collaboration. The Ministry has turned a deaf ear to this plea.

The arguments which resist the suggestion that the Senior Medical Inspector of Factories should be independent of the Chief Inspector are outlined in paras. 32 and 33, but those supporting the proposal are not given. The gist of the committee's argument is that "the activities have to be fully integrated and co-ordinated and that can only be properly achieved if, in the last resort, there is one responsible person at the head of the whole Inspectorate, namely, the Chief Inspector of Factories". If the committee are right in their contention, the outlook for the comparable department in France is bleak. When a medical inspectorate of factories (under a slightly different title) was formed there in 1947, it was put under a Chief Medical Inspector (du Travail et Main-Oeuvre) in parallel with the existing Chief Inspector of a department which had existed since the 1870s. It would not surprise us to learn that the system works very well.

In this inquiry the views of the lay inspectorate on the place of the doctors in the organisation have evidently carried more weight than the views of the doctors them-

2. Kubie, L. S. Neurotic Distortion of the Creative Process. Kansas, 1958.
3. Duties, Organisation, and Staffing of the Medical Branch of the Factory Inspectorate. Cmnd. 736. H.M. Stationery Office. 1959. Pp. 11. 9*d*.

selves. Their success in limiting doctors to the "technical" side is the more ironical because members of our profession, beginning with Sir Thomas Legge, have done more than others in this department to put it on the national and international map. One of the greatest of Chief Inspectors of Factories, Sir Arthur Whitelegge, was himself a doctor; and perhaps the simplest way of getting over the present difficulties would be to make this a precedent for the future.

PREJUDICE AND THE CANCERS

Advances against the citadel held by the cancers are taking place on four broad fronts. There is the basic research in the laboratory, ranging from fundamental problems of cell-division to the composition of tobacco-smokes. There is the clinical research into the ways and means of improving the lot of individuals, with its medical, surgical, and radiotherapeutic tactics. There is the epidemiological approach, typified by the statistical inquiries into the ætiology of lung cancer. And there is the educational front, whose purpose is to improve knowledge, reduce prejudice, and foster early treatment.

The Manchester Committee on Cancer—a voluntary body founded in the 1920s—scored its first success in helping to elucidate the carcinogenic factor in mule-spinners' cancer, now happily under control. After the war the committee entered untrodden territory with an inquiry into the rationale and results of cancer education. For many years previously, of course, cancer education had been developed as a special form of health education by pioneers such as Lombard of Massachusetts, Griswold of Connecticut, and, almost alone in this country, Malcolm Donaldson. But no attempt had been made at controlled experiments, comparing results in similar areas one of which was subjected to cancer education and the other was not. Nobody had tried to assess the causes of delay in seeking treatment and thus to base the methods of approach on sound grounds. And no inquiries had been made into the depths of public ignorance and prejudice about the cancers or into the changes following an educational campaign. All these things the Manchester committee were pioneers in attempting, and many of the published results have already proved valuable. For instance, knowledge has been gained on the level of information among the public,[1 2] and it has been shown that the causes of delay in seeking treatment vary with the site—or at least that in uterine cancer a main factor is ignorance while in mammary cancer it is fear.[3 4] The belief that instruction about cancer necessarily produces cancer phobia has been dispelled, as has the bogy of "flooding of doctors' surgeries" as a result of it.[5] Recently the first statistical results from the "educated" and the control areas showed that after three years' intensive cancer instruction the proportion of women with breast cancer seeking advice in under one month had risen from 28% to 38%, whereas no such change was seen in the comparable control area.[6]

The latest development has been a two-day experimental Teachers' Conference on the theme "Making cancer ordinary . . ." [7] In his closing address Dr. Ralston Paterson said that "the big surprise was that the conference so largely concerned itself with how soon and how best to start instruction, rather than whether it should be given at all." To many the idea of teaching schoolchildren about the cancers is somewhat repugnant, but the teachers present clearly accepted the view of Mr. John Wakefield, the executive officer in charge of the educational side of the committee's work, that "the question we should ask is not 'dare we give older children information about cancer?' but 'dare we take the risk of depriving them of the knowledge that may later save their lives?'".

The suspicion grows that on this subject our own profession is lagging behind public opinion instead of leading it.

REPEATED SNAKEBITE

ONCE bitten twice shy does not seem to be true of many who habitually handle snakes. Martin [1] recorded the case of a snake-charmer who was bitten on many occasions by the Australian tiger snake—probably the most dangerous land-snake in the world. Jutzy et al.[2] reported that a herpetologist in the Panama Canal zone had been bitten on some twenty occasions. Ironmonger [3] claimed to have been bitten forty-nine times. Not unnaturally, many snake-handlers come to regard themselves as immune. Parrish and Pollard [4] have lately reported an investigation to determine whether repeated bites by North American pit vipers resulted in immunity or allergy or had no effect on the result of subsequent bites. They studied 14 patients who were professional herpetologists, snake-handlers, wild-animal dealers, or biologists. 1 subject had experienced twelve envenomations, another ten: the remainder had received two to six bites. Parrish and Pollard found no evidence of immunity developing. Sera compared with controls showed no significant venom neutralisation. Of the 14, 6 experienced severe poisoning from the latest snakebite despite three or more previous bites. 5 had permanent local defects as a result of the bites (in 1 due to a neuropathic antivenene reaction). 4 showed hypersensitivity to venom by scratch tests, though none had experienced anaphylactic reactions after bites. Parrish and Pollard conclude that the severity of repeated snakebites depends on the characteristics of the individual bite and not on the cumulative effects of previous bites.

These findings could be anticipated from antivenene production. Snake venom is a poor antigen compared with diphtheria or tetanus toxin. Immunity in animals rises slowly, and even after several graded inoculations unexpected deaths are not rare. In some animals virtually no immunity develops. Frequent booster doses are needed to maintain immunity, which may drop to zero within three months in dogs [5] and two months in horses when rested.[6] Antiserum effective against diphtheria, tetanus, or snakebite toxæmia must be given in large doses—much larger than a human being could tolerate. Parrish and Pollard attributed the lack of permanent immunity primarily to long and irregular intervals between envenomations. They give scant consideration to the venom dose; but, of all the many variables in bites from poisonous snakes, the venom dose is paramount in determining the outcome. Many do not realise that

1. Paterson, R., Aitken-Swan, J. *Lancet*, 1956, ii, 857.
2. Paterson, R., Aitken-Swan, J. *ibid.* 1958, ii, 791.
3. Aitken-Swan, J., Paterson, R. *Brit. med. J.* 1955, i, 623.
4. Paterson, R. *Canad. med. Ass. J.* 1955, **73**, 931.
5. Wakefield, J., Davison, R. L. *Brit. med. J.* 1958, i, 96.
6. Aitken-Swan, J., Paterson, R. *ibid.* March 14, 1959, p, 708.
7. Report on Teachers' Conference, Disley, March 14–15, 1959. Manchester Committee on Cancer. Educational Project, 558, Wilmslow Road, Withington, Manchester, 20.

1. Martin, C. J. *in* System of Medicine (edited by T. C. Allbutt and H. D Rolleston). London, 1907.
2. Jutzy, D. A., Biber, S. H., Elton, N. W., Lowry, E. C. *Amer. J. trop. Med. Hyg.* 1953, **2**, 129.
3. Ironmonger, C. J. *Pacif. rur. Pr.* 1889, **38**, 67.
4. Parrish, H. M., Pollard, C. B. *Amer. J. med. Sci.* 1959, **237**, 277.
5. Essex, H. W., Markowitz, J. *Amer. J. Physiol.* 1930, **92**, 345.
6. Kuwajima, Y. *Jap. J. exp. Med.* 1953, **23**, 299.

poisonous snakes often bite without injecting significant venom—poisonous snakebite is not synonymous with snakebite poisoning. Judged by venom yields in captivity and by toxicity to animals, most venomous snakes are potentially lethal to mankind; yet, as Reid [7] found, the mortality is surprisingly low. Fortunately, snakes are naturally timid, and biting humans is a defensive measure. Parrish and Pollard excluded bites which did not result in venom poisoning. Even so, of the total of sixty-four bites, twenty-eight—nearly half—were followed by only slight poisoning. It can be assumed, that when people accustomed to handling snakes are bitten it will be rare for much venom to be injected. But such is the toxicity of most snake venoms that a small fraction of their potential venom yield can make the difference between a trivial effect and death.

THE PROTRUDED DISC

IN the twenty-five years since Mixter and Barr [8] identified protrusions of the nucleus of the intervertebral disc as a cause of sciatica, the clinical features of disc protrusions have become well established. The factors associated with changes in disc structure and consequent extrusion [9] have been studied by Charnley [10] and Hendry.[11] It is customary to distinguish the degenerative changes of ageing in the disc from the changes accompanying protrusion; it is uncertain at the moment whether these represent two distinct processes, but it seems that both in ageing and with protrusion disturbances of the fluid balance of the disc play an important part.

The nucleus of the disc can probably be protruded at any point on its circumference, or even into the vertebral bodies themselves; but it is the posterolateral lesion that commands most attention. In the production of back pain, disc tension is a major element [12]; and damage to the posterior annulus and posterior longitudinal ligament may play contributory parts. The cause of the sciatic pain is less easy to determine, but Smyth and Wright [13] have thrown light on this. During laminectomies for prolapsed intervertebral discs they passed nylon loops around the affected nerve-root and attached other loops to the dura mater, the ligamentum flavum, the interspinous ligament, and the annulus fibrosus. Only by gentle root traction could sciatic pain be produced.

There can be little doubt that the symptoms associated with disc protrusion subside rapidly in many patients, but whether the disc heals is less clear. Lindblom and Hultquest [14] and Eckert and Decker [15] have described vascularisation and fibrosis of the nucleus pulposus, but we do not know whether this is a sign of disc repair or of the absorption of abnormal disc material. The protrusion may persist in some patients despite the subsidence of symptoms.[16] Probably about a third of patients with a first attack of sciatica due to disc protrusion can expect complete relief with conservative treatment, and freedom from further attacks. In the remainder symptoms may persist even with rest and immobilisation, or may recur later. These patients are rarely helped by traction or manipulation, and sometimes their condition is made much worse. In this group surgical treatment must be considered.

The operative treatment of disc prolapse is normally confined to simple removal of the displaced part of the nucleus and curettage of the disc space, which is followed by early ambulation. Burns and Young [17] found that 80% of their patients had no symptoms when reviewed a year or more after the operation: and Eyre-Brook [18] likewise reported that a high proportion of patients had slight or no residual symptoms. Reynolds et al.[19] are rather less sanguine about their results, but these still compare favourably with any series treated conservatively.

The success of disc surgery seems to depend on two main factors. The first is correct preoperative diagnosis —patients without a definite protrusion are rarely helped by laminectomy, even if a degenerated disc is curetted. In diagnosis myelography will occasionally help, particularly in the uncommon cases where the third lumbar disc is protruded. The second factor is a wide operative exposure. There is little evidence that a formal laminectomy weakens the back, and it certainly aids inspection of the lower two lumbar discs; simultaneous protrusion of both these discs is not uncommon.

If the disc is degenerate but not extruded, or if the nerve-root is adherent to an old scarred disc lesion, spinal fusion may be considered. Wiltberger [20] favours an inter-body fusion; but the operation is difficult, and ankylosis is uncertain. Posterior fusion is usually more satisfactory, but may be difficult after an extensive laminectomy. While fusion may relieve the back pain associated with disc degeneration, it can hardly affect the sciatica. Charnley [21] has shown that on raising the leg the nerve-root moves extensively; and there is little doubt that this, rather than the movements at one segment of the spine, gives rise to sciatic pain. Patients with backache and sciatica but without definite physical signs or definite disc protrusion are rarely helped by operative treatment. It is because of the poor results in such patients who have been operated on that the value of disc surgery has been questioned.

FALLOUT

To those who fear that the testing of nuclear weapons may already have released enough radioactive material to do considerable harm, the Prime Minister's recent statement [22] and the subsequent exchanges in the Commons last week give little comfort. Since May of last year there has been an increase in the rate at which strontium 90 and other isotopes have descended on this country, and the rate of deposition in rainfall has approximately doubled. The wet summer accounted for part of this increase, but later, when rainfall was more normal, the rate of fallout was still high. The amount of strontium 90 in human diet in the United Kingdom rose much less in 1958 than the rate of deposition, perhaps because heavy rain washed strontium from herbage into the soil; but some of it can still be absorbed thence by growing crops and ultimately find its way into human bones. Bone samples taken early in 1958 showed only a slight increase in strontium 90 over corresponding figures for 1957; but there seems little doubt that later samples will contain more strontium.

7. Reid, H. A. *Brit. med. J.* 1957, ii, 26.
8. Mixter, W. J., Barr, J. S. *New Engl. J. Med.* 1934, **211**, 210.
9. See *Lancet*, 1958, i, 1214.
10. Charnley, J. *J. Bone Jt Surg.* 1951, **33B**, 472.
11. Hendry, N. G. L. *ibid.* 1958, **40B**, 132.
12. Hirsch, R. *Acta orthopæd. scand.* 1951, **20**, 261.
13. Smyth, M. J., Wright, V. *J. Bone Jt Surg.* 1958, **40A**, 1401.
14. Lindblom, K., Hultquest, G. *ibid.* 1950, **32A**, 557.
15. Eckert, C., Decker, A. *ibid.* 1947, **29**, 447.
16. Falconer, M. A., McGregor, M., Begg, A. C. *J. Neurol. Neurosurg. Psychiat.* 1948, **11**, 13.
17. Burns, B. H., Young, R. H. *Lancet*, 1947, ii, 623.
18. Eyre-Brook, A. L. *Brit. J. Surg.* 1952, **39**, 289.
19. Reynolds, F. C., McGinnis, A. E., Morgan, H. C. *J. Bone Jt Surg.* 1959, **41A**, 223.
20. Wiltberger, B. R. *ibid.* 1957, **39A**, 284.
21. Charnley, J. *Lancet*, 1957, i, 186.
22. See *ibid.* May 9, 1959, p. 983.

Special Articles

COST OF PRESCRIBING

Report of Hinchliffe Committee

THE Committee* on the Cost of Prescribing (the Hinchliffe Committee) were appointed by the Minister of Health in June, 1957, with the following terms of reference: "having regard to the increase in the cost of prescriptions issued under the National Health Service, to investigate the factors contributing to this cost and to make recommendations." A separate committee were appointed by the Secretary of State for Scotland to inquire into prescribing costs in the general medical services and in the hospital and specialist services in that country, and their report [1] appeared last month. The Hinchliffe Committee were concerned primarily with practice in the general medical services, but they considered themselves free to deal with any aspect of the hospital service which, in their view, had a bearing on the prescribing habits of general practitioners. They examined written and oral evidence; and an interim report [2] was published in June, 1958, which dealt mainly with means of providing doctors with information of value in their prescribing. The final report [3] appeared on Wednesday and we publish below extracts from the summary of its main conclusions and recommendations.

There was no evidence of widespread and irresponsible extravagance in general practitioners' prescribing, but there was scope for economy; some waste was involved in the present tendency to order larger quantities on each prescription.

THE DRUG BILL

The total cost of the pharmaceutical service rose considerably up to 1951–52. During the period 1951–52 to 1957–58 the rate of increase was less than that for most of the other branches of the National Health Service. Since 1951–52 the proportion of the total cost of the service attributable to the pharmaceutical service has even decreased slightly.

Certain factors had an important influence on costs from year to year.

An influenza epidemic in 1951, the release of chloramphenicol for general prescription, and other factors contributed to the increase up to 1951-52. The rate of increase abated during the next three years due, among other things, to a fall in the cost of dressings, the new shilling prescription charge, and new arrangements for the payment for certain proprietary preparations in frequent demand. The general release of further expensive new preparations, including the tetracyclines and the corticosteroids, together with increases in allowances and fees for retail pharmacists, and the prescribing of increased quantities, added to the drug bill in subsequent years. The main factors influencing the cost of prescriptions were the coincidental introduction of a free and comprehensive Health Service and the discovery and production of valuable but expensive drugs.

The community as a whole derives tremendous benefits from the pharmaceutical service, financially as well as in relief of suffering and saving of life. The use of new drugs has made a valuable contribution in the treatment of tuberculosis and other infectious diseases and in mental practice, and has relieved the pressure on hospital accommodation. The Minister of Health should consider ways and means of publicising these facts.

MEDICAL TRAINING

All medical schools should be encouraged to take an interest in economy in prescribing.

The Minister should invite the Association for the Study of Medical Education to consider the economics of prescribing. Medical schools, where only a minority of students participate in schemes of secondment to general practitioners, should be asked to extend existing arrangements.

There is a clamant need for systematic postgraduate instruction of general practitioners in pharmacology and therapeutics; the average practitioner is unable to judge the validity of the makers' claims for the many new drugs now produced. The appointment of senior general practitioners to instruct junior hospital medical staff in the practical aspects of prescribing in general practice should be considered. Deans and directors should be asked, where appropriate, to consider including in the syllabus for refresher courses instruction about advances in practical therapeutics and the merits and demerits of new drugs and some indication of costs.

New entrants to general practice should be urged to attend a course of one or two weeks' duration, within one year of entering practice. Such courses might be provided by universities and medical schools on behalf of the Ministry of Health and should put special emphasis on problems of prescribing.

GENERAL PRACTICE

Any scheme to limit the range of drugs to be prescribed by general practitioners should involve no loss of efficacy of clinical treatment, should avoid administrative complexities, and should secure substantial savings. There are overwhelming objections of principle and of practice against limitation and no restriction should be imposed on the doctor's right to prescribe whatever drugs he considers to be proper and necessary for his patients.

The main difficulty is the dearth of impartial information on new drugs in convenient and readily accessible form. Adequate information, together with improvements in training and education, is the key to good prescribing.

An independent publication should be established to distribute to general practitioners up-to-date information about new drugs and preparations and the results of clinical trials. The appropriate professional bodies should be asked to take responsibility for producing the new journal, which might be called *Prescribers' Journal*, and which should replace *Prescribers' Notes*, for the medical profession.

Regional medical officers could do more than at present to help doctors in their prescribing. The system of informal advisory visits by regional medical officers should be extended. Regional medical officers should attend seminars and lectures. The possibility of enlisting the help of university departments of pharmacology and therapeutics in the instruction to be given to general practitioners by regional medical officers should be considered.

Disciplinary Measures

The Minister should consult the British Medical Association with a view to tightening the present standards for the investigation of instances of excessive prescribing. Where a general practitioner's costs habitually exceed the local average by more than 50% the case should be referred for investigation by the local medical committee. The penalties for excessive prescribing, particularly where

*The members of the committee were: Sir HENRY HINCHLIFFE, D.L., B.A., chairman, Dr. WILLIAM BROCKBANK, F.R.C.P., Mr. K. R. CAPPER, PH.D., B.PHARM., Dr. H. C. FAULKNER, Dr. F. E. GOULD, Prof. D. V. HUBBLE, F.R.C.P., Prof. C. A. KEELE, F.R.C.P., Prof. M. G. KENDALL, SC.D., Dr. A. M. MAIDEN, Dr. G. F. PETTY, Dr. A. D. STOKER, Sir ARTHUR THOMSON, F.R.C.P. The secretary was Mr. E. L. MAYSTON.

1. Report of the Scottish Committee on Prescribing Costs. H.M. Stationery Office, 1959. See *Lancet*, May 2, 1959, pp. 926, 936.
2. See *ibid.* 1958, i, 1376.
3. Final Report of the Committee on Prescribing Costs. H.M. Stationery Office, 1959. 6*s*.

doctors prescribe extravagantly in order to attract patients, should be severe.

General Advice to Practitioners

Official titles should be used on prescriptions in preference to proprietary names. Prescribers should endeavour to use such titles even when they are longer or less readily memorised than proprietary names. When prescribing by brand name, the prescriber should be convinced of the preparation's superiority by private experience or published evidence and not by unsubstantiated claims by the makers. The Ministry or other body concerned should inform prescribers as soon as economies are likely to result from using official titles for individual preparations. Doctors should not prescribe expensive, elegant preparations when simpler preparations of the same drug are available; and they should refrain from prescribing unnecessarily elaborate polypharmaceutical preparations.

Information should be supplied about prices of *National Formulary* and analogous preparations, classified by therapeutic groups and, wherever practicable, doctors should select from the appropriate group the least expensive of the effective drugs available.

There should be no ban on the prescribing of new drugs but, until the results of clinical trials are known, doctors should only prescribe new drugs when existing drugs have failed.

Quantities

The Minister should seek to reach agreement with the professional bodies concerned on the voluntary limitation of the amount of drugs to be supplied on one prescription to one week's supply or less, with exceptions in chronic or particular cases. Such an arrangement should run for a trial period of two years. To help general practitioners, the Joint Formulary Committee should be urged to amplify the information contained in the alternative edition of the British *National Formulary* about reasonable quantities to be prescribed.

HOSPITAL AND SPECIALIST SERVICES

The example set by the specialist staff will considerably influence students in their preregistration year and young housemen. It should be an educational obligation on every consultant to exercise a proper economy in his own prescribing for hospital patients.

Hospital medical staff should receive instruction in prescribing costs.

The ultimate responsibility for the continuing care and treatment of his patients rests on the general practitioner and the decision whether to accept the advice of a consultant in a particular case is within the practitioner's discretion. When answering letters from general practitioners or referring patients back to them, consultants should recommend official preparations wherever practicable.

THE PUBLIC

Some patients exert pressure on their doctors to prescribe particular drugs for them but the effect of such demands on the drug bill cannot be measured. Senior doctors and well-established partnerships are generally better able to resist them than young doctors lacking in experience and working on their own. Patients should be asked to cooperate by accepting more readily the doctor's advice and guidance. Posters and notices should be provided for display in doctor's surgeries warning patients against the " medicine habit ".

THE DRUG INDUSTRY

Everything possible should be done to prevent public money being wasted in inflated and expensive publicity campaigns. The industry should be asked to consider with the professional bodies and the Minister whether anything further can be done to maintain the highest standards and limit the more extreme forms of advertising.

Competition, when the period of patent protection of a proprietary preparation expires, may bring down the price and should be encouraged. The Minister should consider with the industry and with the medical and pharmaceutical professions ways and means of limiting the present proliferation of polypharmaceutical preparations.

Firms should be encouraged to increase their research effort. Wider cooperation between all parties concerned in research is called for.

The voluntary price-regulation scheme is making a valuable contribution: it is a considerable step forward that the industry should recognise and accept the need for price regulation. Pricing arrangements between the Ministry of Health and the pharmaceutical industry should be designed to allow fully for genuine research expenditure and to discourage extravagant overheads and sales promotion.

The pharmaceutical firms which do research are making an essential contribution to therapeutic progress. The costs of research on therapeutic and prophylactic products are considerable but are no higher than in other countries making a comparable effort. The conditions which favour profits for research, such as patent rights, the publicising of proprietary names, and the price agreement with the Ministry of Health should be accepted. No changes in the organisation of the pharmaceutical industry could be recommended without a much more detailed inquiry than the committee were able to make.

The drug industry is playing an all-important and progressive role in the development of the N.H.S. and the export trade. The doctors' freedom to prescribe in the N.H.S. inevitably encourages extravagant sales propaganda, some of which is undesirable. The pharmaceutical industry is one which has to face unusual risks. The sudden discovery of a new therapy anywhere in the world can put a product, on which a great deal has been spent, off the market overnight.

CLINICAL TRIALS

Present arrangements for the organisation and interpretation of clinical trials and for publication of the results are inadequate. Better organisation and speedier publication could greatly influence the prescribing practice of general practitioners. New drugs should be subjected to independent controlled clinical trial as early as possible. Hospital authorities should encourage clinical trials and should give those who take part in them time and facilities for the work. Therapeutic research should be regarded as a normal clinical function and not as a remote activity for the select few.

The appropriate professional bodies should be asked to collaborate in the formation of a Clinical Trials Committee which would organise clinical trials of new drugs and preparations and interpret the results. Their findings should be published in the proposed new *Prescribers' Journal*.

The costs of clinical trials should be met by the manufacturers. It is undesirable that doctors should be paid by the manufacturers for participating in such trials. Firms wishing to continue to make their own arrangements for clinical trials should be encouraged to do so.

RETAIL PHARMACISTS

There is no satisfactory alternative to the present system of supplying N.H.S. medicines through the established retail channels. If purchase and distribution of medicines were undertaken centrally or through health centres costs would increase.

The prices which the Ministry pays should be reviewed at regular intervals. Payments to pharmacists should be made as promptly and correctly as possible. Regulations which

impose additional tasks on chemists and increase their overheads should be avoided.

In order to help chemists, doctors should be encouraged to use non-proprietary names, where appropriate; and the industry should be encouraged to rationalise pack sizes and prescribers to order quantities in accordance with the packs available.

The appropriate medical and pharmaceutical organisations should be invited to discuss methods for improving professional collaboration between general practitioners and retail pharmacists.

PRESCRIPTION CHARGES

The present prescription charge is a tax which, besides stimulating the wrong incentives, has proved disappointing financially. If any change in the basis of the prescription charge is contemplated in the future, it should not be put into effect without an attempt to assess in advance its probable effects by means of a special inquiry through a body such as the Social Survey.

If a voluntary limitation of the quantities to be prescribed on one prescription proves to be successful in controlling expenditure on drugs, consideration should be given to the desirability of abolishing the prescription charge altogether.

STATISTICAL INFORMATION

The Minister should make suitable arrangements for obtaining adequate statistical information about prescribing and for the analytical study of this information.

The quality of the data available on prescribing should be improved to enable accurate assessment to be made of the nature and magnitude of the forces tending to increase the drug bill. The Minister should make arrangements for ad-hoc inquiries in selected areas (e.g., into the relative prescribing habits of single-handed doctors and of those in partnership or group practice). A study of the prescribing of new drugs such as the antibiotics and corticosteroids should help to reduce wastage of these very expensive items. A study of the relative roles of proprietary and standard preparations in prescribing under the N.H.S. and of the use of cheaper alternatives should help to effect savings.

GENERAL RECOMMENDATIONS

A permanent expert body, to include men with business experience, an economist, and a statistician, should be appointed to advise the Minister expeditiously on matters affecting costs in the pharmaceutical service.

In the absence of a stock orders scheme, which was not regarded as necessary in England and Wales, an early and substantial increase in the present capitation payment for the supply of drugs for immediate administration should be considered.

The practice of substitution is not a practical or desirable method of securing economies in the drug bill. It removes any incentive on the part of the prescriber to get to know the non-proprietary alternatives to proprietary preparations.

The amount by which the drug bill is inflated by purchase tax payable on proprietary preparations should be noted and publicised every year.

AN INDUSTRIAL MEDICAL CENTRE

S. JENKIN EVANS
M.B. Edin., D.P.H.
SENIOR MEDICAL OFFICER, WILTON WORKS,
IMPERIAL CHEMICAL INDUSTRIES LIMITED

THE new industrial medical centre opened by Imperial Chemical Industries at their Wilton works in Yorkshire is probably the largest of its kind in the world. It caters for 14,000 employees and is equipped not only for ordinary consultations and treatment, but for radiology, ophthalmology, dentistry, chiropody, and physiotherapy. Conviently, the central labour department of the works, dealing primarily with recruitment and welfare, is housed in the same building.

In the entrance hall an illuminated screen shows the layout, and from the central waiting-room, with its inquiry desk (fig. 1), all ambulant patients are routed. Simple signalling systems and internal telephones facilitate intersectional working and rapid flow of patients.

The consulting and diagnostic unit (fig. 2, 11) has two rooms for nurses' interviews and three for doctors' consultations, and each of the consulting-rooms has an examination room and three changing cubicles. A separate diagnostic room includes a soundproof section for audiometry. Electrical diagnostic instruments, eye-testing equipment, and patient signals are operated from a central panel on each consulting-room desk; the automatic height and weight recording apparatus in the nurses' interview rooms, and the urine sampling units are of unique design.

The main treatment room has eight segregated cubicles (some equipped for specialist treatment) with nurses' wash-hand basins and desks centrally placed. This arrangement makes for better contact between nurse and patient, greatly reduces the dangers of cross-infection, and saves the nurses' time.

Beyond this section is a recovery ward of eight beds, and the physiotherapy unit, which in an emergency could provide space for fifty stretchers. A surgical unit dealing with minor injuries includes an immersion bath and sprays for the primary treatment of chemical burns. The entrance for stretcher cases is at the end of the treatment wing beneath a canopy adjoining the ambulance garage. Oxygen is piped to the recovery ward and surgical unit; ultraviolet germicidal lamps have been installed in this unit and in the sterilising rooms and sluice rooms.

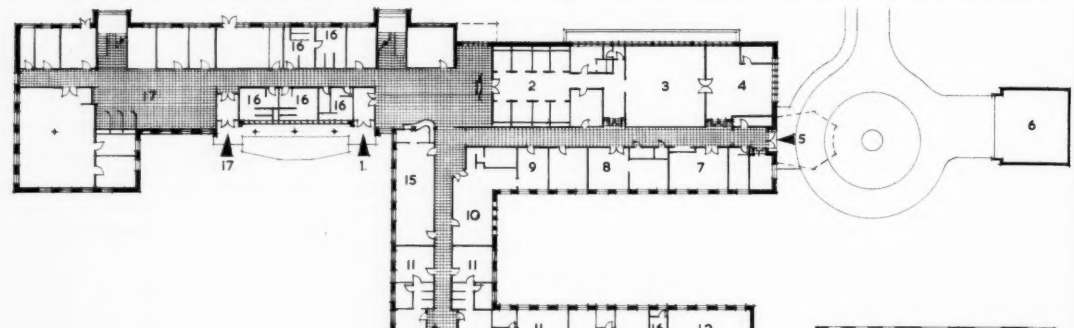
The X-ray unit and the main records office are located between the treatment and consulting wings.

The laboratory accommodates four technicians. Four dental surgeries and associated offices are located on the first floor.

Construction

The two-storey brick building has a steel framework. Since none of the internal walls bear any weight, the internal layout is flexible. Except in the treatment-rooms, the finish is in domestic rather than

Fig. 1—Main reception hall showing inquiry desk and concealed entrance to treatment wing.



FIRST FLOOR

Fig. 2—Plan of the centre. 1. Main entrance. 2. Treatment-room. 3. Recovery-room. 4. Physiotherapy. 5. Stretcher-case entrance. 6. Ambulance garage. 7. Dispensary. 8. Surgical unit. 9. Chiropody. 10. X-ray. 11. Consulting units. 12. Laboratory. 13. Dental units. 14. Conference-room. 15. Offices. 16. Toilets. 17. Labour department entrance.

institutional styles. The floors are of rubber tiles and the walls are papered or gloss-painted. Where possible, the ceilings are acoustic-absorbent, and embody a low-temperature heating system of aluminium perforated panels.

In the treatment areas floors and walls are in terrazzo to door height, and heating is by warmed and filtered air. All rooms, however, have adequate natural ventilation and lighting. In treatment areas 'Clear Story' lighting gives good and even diffusion, while glass door panels and glass bricks have been incorporated wherever possible to give "borrowed" light in passages.

The present floor area of the building is 26,000 sq. ft., of which 6000 sq. ft. is occupied by the labour department.

Staff

The full-time staff includes three doctors, a radiographer, a physiotherapist, two trained medical laboratory technicians, and eleven State-registered nurses, four of whom combine with ambulance-driver attendants, working in shifts to provide a continuous emergency service. Visiting ophthalmologists and an oculist operate recognised National Health Service clinics, and also prescribe safety lenses provided by the company for the protection of employees with gross visual defects. Similarly, the dental unit operates as part of the N.H.S., being placed at the works medical centre for the convenience of employees who choose to use it. At present it has one full-time dentist, but has been designed for three.

During the first year's operation 82,761 attendances were recorded; but this rate will be rapidly exceeded as the site develops and all sections come into action.

Prevention

The medical service based on this centre is essentially complementary to that of the N.H.S. Its purpose is to maintain healthy employees in a healthy environment, the emphasis being on prevention. This naturally requires attention not only to the worker but also to the nature of his work. All employees are medically assessed on engagement, and periodic examination is given to those in potentially hazardous occupations and to other specified groups such as transport drivers, food-handlers, and juveniles.

Many of the day-to-day treatments are undertaken at the request of consultants or general practitioners, with whom liaison is intimate and cordial. A personal medical dossier is maintained for every individual, and patient-doctor confidences are jealously guarded.

Designed by I.C.I.'s architectural and engineering staff, the centre well illustrates the company's farseeing industrial medical policy

Medicine and the Law

Standard of Nursing Care

A NURSING-HOME sued a patient's widow for the balance of their fees—£73—unpaid. By her defence the widow claimed that the services contracted for had not been properly rendered: and she counterclaimed for negligence which she alleged had shortened her husband's expectation of life.

In June, 1954, the patient went into the private nursing-home with cardiac failure, his wife contracting for fees of 35 guineas a week. He had attacks of breathlessness and had his own supply of oxygen by his bedside, using it when he felt the need of it, though his doctors regarded it as a placebo. Shortly before he was due to go home, his cylinder was removed for recharging and was not replaced by the nursing-home, though oxygen apparatus was available in the corridor.

On July 15, his doctors decided on a course of three doses of ammonium chloride combined with mersalyl injections for July 18 and that he be discharged on July 20. On the same day a doctor attending another patient was in error handed the patient's prescription sheet by one of the nurses and prescribed on it 'Pitressin' intended for his own patient. When the nurses discovered the mistake the wrong prescription was cut off the sheet. It was not proved that the first patient was ever given pitressin. The following day the mistake over the prescription was drawn to his own doctor's attention. On that day his doctor wrote down on the prescription sheet detailed instructions for the three-dose course of ammonium chloride as planned, but at the same time gave to the nurse in charge oral instructions to give four doses and postpone the discharge by one day. The nurse, who was going on holiday, wrote into her report the inconsistent oral instructions, but referred those taking over her duties to what the doctor had ordered by the words "see red book". In the event only three doses were administered. During the following weekend the patient suffered from breathlessness and other distress, but the nursing reports did not record any administration of oxygen. He left the nursing-home on July 20 and died at his home on Aug. 12.

The trial judge gave judgment for the nursing-home on the claim and dismissed the counterclaim.

The widow appealed in person, basing her many complaints about treatment on the nursing records and evidence at the trial.

The Court of Appeal allowed her appeal on the claim for the balance of fees, but affirmed the trial judge's decision on the counterclaim, and awarded the widow the costs of the appeal and half her costs in the action.

Lord DENNING said, on the mistake over the pitressin prescription, that even if the doctor should have looked to see whose name was on the sheet given to him, there remained the question: How did it get on to another patient's locker so that it was put before the doctor to sign? Though it was not proved that any harm had been done, no-one could deny the potential danger of a wrong prescription. It was a matter on which the utmost care was demanded and the nursing-home could not withdraw themselves from responsibility for that error.

On the administration of ammonium chloride, the inconsistency between what the doctor had written and what was in the nurse's report would have been discovered if anyone had followed the direction to " see red book ". All the medical and nursing witnesses had agreed that the key document must be the doctor's prescription sheet; but no one appeared to have checked, because everyone had gone by the nurse's report. And if they had discovered the discrepancy surely they would have checked with the doctor. That was another error.

Though no damage had been proved to result from those errors in the records there was also the question of the oxygen. It might not have done the patient any good, but it would have comforted him, particularly as he was recorded as being breathless on several occasions during those critical days. When he had had oxygen by his bedside for such a long time and it was then removed and there was no record of any oxygen being administered, it did seem that the very high standard of nursing and care required would have made him more comfortable by ensuring that he had it.

On those three matters alone his Lordship did not think that the nursing-home had fulfilled the high standard required of it. How much they ought to receive in the circumstances for the services which they had rendered was a question for a jury rather than a judge; but in his Lordship's view the claim should be reduced by the amount still outstanding. There would be judgment for the widow on the claim. Her counterclaim must be dismissed.

Lord Justice SELLERS, concurring, said that good nursing required that if there was a conflict between a written document by a doctor and an oral statement recorded by a nurse, some attempt should be made, before the treatment was administered, to find out what the true position was. Not to have done so was a mistake falling short of the standard of care and skill expected of a home of this sort.

On the oxygen, one would think, having regard to the standard to which the patient was accustomed, that, without any request by the patient or his wife, oxygen would have been provided automatically to replace his own supply. It might appear a trivial matter, but satisfactory nursing and the comfort of a patient might very often depend on personal idiosyncrasies or wants being supplied and detailed and very careful attention to small matters.

Lord Justice HARMAN, also concurring, said that the only way in which the Court could now judge the standard of nursing was by looking at what had been written down by the nurses at the time, for in the witness-box these girls—and they were little more—did not remember anything at all about the matter. That was not unnatural, since this patient had had no fewer than 13 nurses during his month at the home. There were other minor matters in the records which were all symptomatic of the way in which the contract to perform nursing of a first-class quality in a first-class way had not here been fulfilled.

LONDON CLINIC TRUSTEES *v.* HOARE. *Court of Appeal:* Lord Denning, Sellers, and Harman, L.JJ. May 4, 1959. Lady Hoare in person: Counsel and solicitors: Roger Ormrod, Q.C., and Michael Parker (Layton & Co.).

M. M. HILL
Barrister-at-Law.

Points of View

MURDER AT THE CROSS-ROADS
or the
Decapitation of General Practice

ERICH GEIRINGER
M.D. Lond., Ph.D. Edin.

SINCE the end of the war Britain has set out to evolve a society in which social justice and political freedom can exist side by side. The National Health Service is one of the cornerstones of the new order. It gives all members of the community free access to all diagnostic and therapeutic facilities. Though there may be some doubt whether the emphasis on the absence of individual payments is indeed the best way to secure equal and just apportionment of the nation's remedial resources, few will deny that financial hardship to patients was widespread before the advent of the health service; or that its introduction was a source of great satisfaction to the majority of the people and must for this reason be reckoned an important factor in the social and political stability of the country.

The N.H.S. has now been in existence for ten years, and one can discern some of its successes and some of its failures. This paper attempts to analyse one of its major flaws—the payment of general practitioners by capitation fee.

Most doctors in most countries at all times have been paid by fee for services rendered. The adoption of this method by the N.H.S. met with two main objections—that it would be cumbersome to administer and that it would be open to abuse. There may also have been an unexpressed fear that a fee-for-service system, even if unabused, would tend to be expansive and therefore expensive. This well-tried and logical method was therefore discarded in favour of the capitation fee, a relative newcomer to the scene and one whose long-term effects, when it was applied on a nation-wide scale, nobody could foretell.

Under the per-capita system, a practitioner undertakes to provide medical care in consideration of a fixed annual fee per person. If this fee were very large and all doctors fully competent and conscientious, such a system could theoretically provide a perfect medical service; but when the fee is an economic one and the doctors are a heterogeneous collection of mainly ordinary people with variable skills and no overwhelming desire for self-sacrifice, payment by capitation must encourage them to do less and less for more and more patients. This trend has found widespread expression in the past ten years and its manifestations may be considered under three heads: the bad practice, the utility practitioner, and the hospitalisation of medicine.

The Bad Practice

This type of practice falls below all reasonable professional standards. It is conducted from antiquated and badly maintained premises where patients wait in uncomfortable surroundings to see a doctor who only rarely consents to give even a perfunctory examination; he never makes any investigations and hardly ever initiates one. His referrals to hospital are non-specific, and accompanied by only the scantiest information. His equipment is outdated. His treatment consists in the indiscriminate renewal of a dozen standard drugs and mixtures. He keeps no proper records.

The less said about this type of practice the better. When Collings published his illuminating survey of general practice [1] he made the tactical mistake of describing in all their degrading detail some of these bad practices which are still common in industrial Britain. The subsequent discussion was swamped by consideration of this least important of his contributions.

This kind of practice originated at the turn of the century, partly from genuine attempts to provide some kind of general-practitioner service for the poor, partly as a result of the panel system. But, though the N.H.S. cannot be said to have brought these practices into existence, it should have made their continuation impossible. Under the per-capita method of payment this type of pauper medicine is still profitable, and is no longer, as formerly, confined to the poorest section of the community.

There are several methods by which the N.H.S. could be cleared of these shameful relics; but the natural and surest way would be a fee-for-service system which would eliminate them within a few years. The importance of this type of practice to the wider problems of the fate of British medicine is, however, no greater than that of the rash of an exanthematous disease: it is widespread and has a characteristic distribution, it is ugly, and it helps in diagnosis; but it constitutes neither the essence nor the danger of the disease.

The Utility Practitioner

The utility practitioner is competent, honest, and hard-working. Having accepted the realities of the N.H.S., he tries to make the best of it for himself and his patients. The utility practitioner aims to have as many patients as possible and to give each a just proportion of his time. His patients wait in adequate rooms; their complaints are listened to and they are examined when necessary. Simple tests such as urinalysis are performed, and sometimes even hæmoglobin levels are estimated. A case needing further investigation is referred to hospital. Simple medical treatment is conscientiously prescribed, but this is the limit of therapeutic intervention.

The numerous psychoneurotics are a great worry to the utility practitioner. He cannot spare the time to listen to these cases; they come every day and " there is nothing wrong with them ". He considers himself lucky when one of these patients, dissatisfied with the scant attention he receives, decides to change his doctor, and he is careful not to accept such patients if he can spot them in time. Altogether he is not happy to have on his list people who are ill, and, although he will often accept them from a sense of duty, he considers it unfair that people should only sign up with him when they fall ill. Whichever way he looks at it, there is no denying that his favourite patients are those who have never any need of his services.

Pregnant women in his practice go with his blessing to the nearest antenatal clinic, and babies to to the infant-welfare clinic; he feels no grudge against the activities of school and works doctors. Minor surgery is in his opinion better done at the casualty department of the local hospital, and he himself has ceased to do any long ago. The eyes and ears of people are too precious to be played around with by a mere G.P., and he gladly refers such cases to the special departments. He feels that a consultant who is asked for advice should be asked for " advice *and treatment* ". His motives in thinking that a gynæcologist or a dermatologist will do the patient more good than he himself are above reproach. The more often he refers patients in this manner, the more his own knowledge and skill shrink and the more justified his self-depreciatory attitude becomes. In the evening and at weekends many a utility practitioner hands over his responsibilities to a privately run " emergency service " (N.B., the new definition of emergency is not a condition threatening life but one threatening the G.P.'s evening off), for he does not see why he should " kill himself ".

The utility practitioner has evolved a rudimentary type of general practice, shorn of " frills and fancies ", eschewing unremunerative responsibilities as far as possible. Within these narrow limits he is competent but rarely happy. Together with his skill he has had to jettison most of the fascination of the exercise of general medicine. His relationship with his patients is superficial and discontinuous and therefore poor in human satisfaction, and he plays second fiddle to his colleagues in the hospital service. His son, if he can help it, is not going to be a G.P., not in Britain anyway.

Hospitalisation of Medicine

This process, which has advanced to a frightening degree in a short time, has an active and a passive component. The active component has just been described; it consists in the deliberate referral to hospital of conditions which at other times and in other climes have been and are still the province of the general practitioner. The trend is conditioned by the economic structure of the N.H.S. with its marginal capitation fee for G.P.s on the one hand and the unlimited liability of the hospital service to deal with referrals on the other. As hospitals are gradually expanding to deal with this type of work, building up specialised departments and engaging specialised staff for the purpose, a vested interest is created. This in turn produces a change in public opinion, so that after a surprisingly short time the voluntary surrender of responsibility on the part of G.P.s becomes an almost irreversible custom against which individual practitioners hold out at their peril.

Minor surgery may serve as a case in point.

Every year there are about $11^1/_2$ million attendances at casualty departments in this country. Most of them are minor injuries and infections, cut fingers, abscesses, whitlows, and the like, requiring minor surgery and sometimes certain medicaments. The patients either arrive of their own volition or are sent by their G.P.s. Why are they not dealt with by their own doctor? It might be argued that they receive better care at the hospital, but this is often demonstrably untrue. Usually, after they have waited for a long time, the simple diagnostic and therapeutic procedures required are carried out by newly qualified house-surgeons or even by students with the help of a student nurse. Although this type of surgery is simple, experience is valuable. In the casualty department the young doctor acquires this experience and then passes out into general practice, in most cases never to use it again. He would gladly deal with such cases in his own practice, as his colleagues in other countries do; but he is working under a system which makes such activities economically undesirable. His skill atrophies, patients assume that this type of case should be treated in hospital, and hospitals begin to clamour for new casualty departments.

1. Collings, J. S. *Lancet*, 1950, i, 555.

The time must come when even a skilled and well-equipped G.P. will be risking his reputation when he treats such a case. If anything goes wrong he will be blamed for not sending the case to hospital. Yet the retention of this type of case by the G.P. appears to be desirable. It would add diversity to his work, create more continuous contact with his patients, and help him to retain basic skills and knowledge. Patients would have prompt attention near their home by an experienced doctor with balanced judgment. Hospitals would be disencumbered of thousands of trivial cases which every day interfere with their proper function. The medical profession would benefit by the closer link between G.P.s and hospital doctors—i.e., by lessening of the ever-widening gap between members of the same profession who have received the same basic training.

These considerations apply to a number of other activities which N.H.S. practitioners have tended to hand over to hospitals and clinics. They include antenatal care of normal pregnancies (345,000 women attending antenatal clinics in 1957 in England and Wales); normal deliveries, simple infertility investigations; cauterisation of cervix; child health (9,800,000 attendances by children under five at clinics in 1957 in England and Wales); care of acute systemic infections such as pneumonia and bronchitis; electrocardiographic examinations; much of diagnostic radiology; circumcision; care of the moribund; and, last but far from least, minor psychotherapy. All these and many more items of medical care have passed out of the grasp of the N.H.S. practitioner into hospital medicine. It is particularly ominous that the very foundation of general practice, the care of mother and child, which one would have thought to be the most jealously guarded part of a family doctor's work, is being taken over in a wholesale fashion by the clinics.

The progressive hospitalisation of British medicine has, however, a passive component, not dependent on deliberate avoidance of duty on the part of practitioners. This process works insidiously and cannot be guarded against as long as payment by capitation continues. It constitutes by far the greatest danger and threatens to abolish general practice in all but name.

The dynamics of medical progress produce a constantly changing relationship between hospital and general practice, apportioning their respective share of medical care. For the past hundred years most of the important advances in the investigation and treatment of disease have necessarily arisen from the cooperation of teams of pure scientists, medical research-workers, and hospital clinicians. As new methods become available, patients are drawn from their family doctor into the hospitals and "home diseases" tend to become "hospital diseases". Hypertension, diabetes, the pneumonias, coronary-artery disease, and rheumatoid arthritis are examples.

While this takes place, general practice is impoverished; but as the exact indications and limitations of new procedures are worked out, and especially as new generations of medical students are made familiar with their application, there is a tendency for G.P.s to apply these new methods, and for the diseases in question once more to be treated outside hospital. In this way general practice is enriched and rejuvenated and kept abreast of modern developments.

In using new procedures the G.P. has to overcome not only the inertia against change, and the financial obstacles of acquiring new knowledge and new equipment, but also the vested hospital interests. Specialists naturally tend to hold on to new methods and to feel that the time has "not yet" come when they may be safely entrusted to the G.P.—nor is to be expected that they should relish the idea of their supply of cases, which forms the nucleus for further advances, melting away into the scattered practices of the family doctors.

Where doctors are paid for what they do, and are not paid for what they do not do, the tendency to adapt modern methods to general practice is strong because it is based on economic necessity. In the other countries of the free world, large numbers of G.P.s do their own diagnostic radiography and their own electrocardiography, supervise anticoagulant and steroid therapy, stabilise the hypertensives, diabetics, and epileptics in their practices, and treat cases of coronary thrombosis and of pneumonia at home or in the local hospital. In these circumstances close personal cooperation becomes a necessity for both the practitioners and their specialist colleagues; the resultant integration of the medical profession presents a happy contrast to the present state of affairs in Britain.

Under the capitation system, while the obstacles to the transfer of modern methods from hospital to general practice remain the same, the incentives to such a transfer are entirely lacking. The introduction of a new activity into a busy practice can only result in financial loss. The outlay, for example, in time and money which would enable a N.H.S. practitioner to do his own electrocardiography and keep up with important developments in this field would be economically unjustifiable, and in fact only an infinitesimal fraction of N.H.S. practitioners are quixotic enough to undertake such investigations. As a result, coronary-artery disease remains a hospital disease, which is not in the best interests either of the patients or of the medical profession as a whole. In private practice, of course, electrocardiography is commonplace, and the majority of such cases are treated in their own homes.

In other words the natural interchange between general practice and hospitals has become a one-way traffic. Every day general practice loses something to the hospitals, and, apart from the introduction of new drugs, gains nothing. Thus it has come about that in Britain we have the most restricted and the most out-of-date form of general practice to be found in any of the English-speaking countries.

That the capitation system allows the "Collings" type of practice to flourish, and that it encourages the utility practitioner, is relatively unimportant. Every system has its peculiar abuses, and the negative "rackets" within the N.H.S. have their full and no less repulsive counterparts in the positive racketeering to be found in private practice and under fee-for-service systems. The real tragedy of the present situation lies in the relentless process of passive hospitalisation which forces even the best practitioners into doing bad general medicine. How bad no-one can realise who has not seen how a competent and keen family doctor works nowadays in other countries—practising modern medicine in modern surgeries with clerical and laboratory help, choosing consultants personally, and retaining full charge of patients even when they have to go to hospital. He wields great influence in the medical community and is on terms of equality, both socially and medically, with his hospital colleagues. In Britain G.P.s may be unable to obtain X-ray examinations of their patients unless the request is first endorsed by the local outpatient department (staffed largely by recently qualified doctors). This may be taken as a measure of the

gulf which is widening between practitioner and hospitals in Britain and between general practice in Britain and in the rest of the free world.

It would not be in accordance with facts to suppose that hospitalisation of medicine started only with the introduction of the N.H.S. The process was well under way by 1948, largely as the result of the "panel" system. The N.H.S. could have reversed or at least halted this trend. Instead, it has set the seal of approval on the gradual extinction of the family doctor.

Is General Practice Really Necessary?

This question deserves careful consideration. The British have a peculiar and historically very successful way of bringing about the most far-reaching changes of substance with minimum alteration of form and nomenclature. We may therefore expect that, if present trends continue, long after the work of G.P.s has ceased to be either general or practical they will still function under this designation and will be referred to in leading articles as the backbone of the profession. In reality they will have become the little-regarded signers of certificates and signposts to the nearest hospital.

Theoretically this may not appear incompatible with a healthy medical system. The only sacrifice involved, it might be argued, would be the rather shadowy benefits of personal relationship and continuity of care. In exchange one can envisage highly developed outpatient departments where intensively rationalised investigations and treatment and immediate specialist attention would be available. These departments might at the same time absorb and rehabilitate the local practitioners. Home visits could be organised from the hospitals. We may yet seem far from such a state of affairs, but the G.P. clinics which have lately sprung up, and the Cambridge pædiatric experiment, are promising beginnings.

Few responsible doctors would care to recommend publicly such a virtual abolition of general practice, but almost all responsible doctors are actively engaged in bringing it about. The consultant who "consults" in the absence of the patient's practitioner, the senior registrar who prescribes for the practitioner's patients, the registrar who admits cases that should be treated by the practitioner, the house-surgeon who lances abscesses in the casualty department, the professor who advocates bigger and better antenatal clinics—they are all busily engaged in destroying general practice. To say nothing of the G.P.s themselves, who under the present system are forced actively or passively to connive at their own degradation.

Can they all be wrong, or are they perhaps assisting to bring about a beneficial and historically necessary change? Is general practice perhaps an outmoded form of medicine unsuited to modern life and to modern medical methods?

This paper is written on the assumption that general practice is worth preserving. So I shall briefly state the main reasons which have led me to this conclusion.

Many people feel the need for an outsider whom they know and trust, and on whose judgment they rely, to unload their physical, mental, and spiritual anxieties and doubts. A good G.P. answers this need whereas the hospital service could do so only with difficulty and imperfectly. To the extent to which G.P.s fail to inspire the necessary confidence, or are unable to spare the necessary time, people will turn to the extraprofessional councils of faith healers, spiritualists, and nature curers. To ignore this real need would be wrong.

Secondly, the increasing complexity and specialisation of medicine has made it more than ever desirable that the final responsibility for the conduct of a case in all its varied aspects should remain in the hands of one doctor. At every stage he could make his decisions with full knowledge of all the personal and medical factors involved and could integrate the findings of the specialists. Apart from being in the interest of good medicine, the presence of such an arbiter can do much to eliminate friction and imaginary grievances. The absence from the medical scene of practitioners filling this role efficiently is one of the badly felt deficiencies of the present system.

Again and again one finds that nobody seems to be responsible for the conduct of a case, the practitioner relying on hospital agencies who have taken over de facto, the hospital relying on the practitioner whose case it remains in theory, and the patients floundering without clear guidance and sometimes even with contradictory advice. The old principle of "one patient one doctor" has been all but abandoned at the very moment when its intelligent enforcement could bring the greatest benefit.

The existence of healthy and independent general practice exerts a constant pressure on the hospital services, tending to keep them efficient and humane. In a service which is constantly changing and advancing, such outside pressure is indispensable. It cannot, in the nature of things, be effectively applied by lay agencies. General practitioners should work under a system which allows them to take a personal interest in their patients, to have leisure to follow their cases into hospital, to confer on the spot with their hospital colleagues, and to have freedom to choose consultants. Such a body of practitioners is the best safeguard against hospital services becoming complacent, inefficient, and even dangerous. Under the N.H.S. as at present constituted the G.P. is usually only too grateful when the hospital takes a case "off his hands"; he has no leisure to follow his cases into hospitals, and he is hardly likely to question too much the activities of those who do so much of his work for him. His professional status has declined to such an extent that what suggestions he may have to make command little attention.

Under the present system, consultants acquire, on their appointment, freedom to stagnate professionally for the next twenty-five years with absolute impunity. The only way in which control of their standards would be practicable and acceptable is that it should be exerted by a healthy body of G.P.s, who should have every opportunity to dispense with the services of specialists who fail to command their confidence. A consultant's earnings should depend on the number of times he is called in to consult, and he should not be able to delegate consultation. None of this can come about in the present debilitated state of general practice. Except for the indirect influence of the teaching hospitals, and the clumsy interference of the lay administration, the hospital service is thus left to itself without an informed body of outside critics who can bring effective pressure to bear. The result is stagnation and a decline of standards, punctuated by sharp outcries when some particular ineptitude manages to penetrate to public consciousness. The absence of G.P.-hospital rivalry and criticism may have a superficial appeal to the committee mentality which runs the N.H.S.; but it is a sure symptom of decline. Notoriously, doctors tend to differ; and, however distressing such differences may be at the time, in the long run they are the only safeguard of continued advance in the right direction.

There remains a function of the general practitioner which, in modern society, far outweighs in importance all those mentioned so far. When hospitals are financed by the State, and hospital doctors employed on a salaried basis, the existence of a strong, healthy, and prosperous general practice becomes the only guarantee of the continued freedom of the medical profession. As long as general practice provides an interesting, remunerative, and honourable alternative to hospital work, doctors in hospitals will feel free to criticise, to take initiative, to stick up for their own ideas. When general practice is as weak and contemptible as it is becoming in Britain, doctors cling desperately to their hospital appointments and become toadies, fearful lest they should be cast into the outer darkness of general practice; they become an easy prey to official manipulation and domination. When the N.H.S. was introduced, the profession, anxious for its freedom, resisted plans for a whole-time salaried service; but since general practice has become an unacceptable alternative to most hospital doctors, the result is exactly as if they were already working under a whole-time salaried system.

Whether the freedom of doctors is desirable is of course a valid question which one could debate at length. Quite apart from having a personal preference for freedom, I am convinced that good medicine is impossible without the professional freedom of doctors; that the professional freedom of doctors is an illusion without a healthy and independent body of general practitioners and that good general practice is impossible under the N.H.S. as at present constituted.

The Remedies

PRIVATE PRACTICE

After the introduction of the N.H.S. some patients preferred to continue to pay for medical care from their own pockets. Their decision has kept a nucleus of private practice alive which has grown slowly as the drawbacks of N.H.S. practice have become apparent. The main obstacles to a further growth of the private sector of British medicine is the cost of drugs. If this obstacle were removed, the flight among middle-class patients from the capitation practitioners might well develop into a stampede; this flight is unlikely to spread to the working classes, not primarily because they are so much poorer but by reason of different attitudes. The working classes have been used for decades to the panel system, and the idea of laying money aside for health purposes is foreign to them; nor has their education as yet progressed to the point where the majority have a sound idea of what modern medical care should be. The introduction of the Welfare State, with its emphasis on the doling out of benefits rather than on a rise of standards which would enable people to secure benefits for themselves, has not helped in this respect.

The resurgence of private medicine would give an uplift to general practice, and by exerting a healthy influence on the hospital service would be an important safeguard of professional freedom. It would reintroduce, however, the division between pauper or utility medicine and medicine "for the rich". This is wholly undesirable and would defeat one of the most important aims of the N.H.S. It would also produce a corresponding cleavage amongst G.P.s. However, until the N.H.S. is reformed so as to make the practice of good general medicine possible, one can have nothing but sympathy for doctors who are taking the way out into private practice.

HEALTH CENTRES

The N.H.S. was brought in with visions of State-aided health centres in which groups of practitioners would be able to practise up-to-date general medicine. This might have counteracted some of the worst consequences of the capitation system. Even then the positive incentives against sending people to hospital would still have been lacking. In any case these sanguine promises have proved entirely unrealistic. One of the advantages of a fee-for-service system would be that it would induce doctors to build up their own health centres, thus saving public money and providing an outlet for individual enterprise which is the basis of medical progress.

SALARIED SERVICE

Superficially, a salaried service might be thought to provide a remedy for many of the disadvantages under which general practice labours at present. It would abolish the need for head-hunting and would allow practitioners to devote as much time and skill to each case as they deem necessary. It would, not, however, provide them with any overwhelming incentive for doing so. Moreover, a salaried service for G.P.s could not be introduced without taking away the freedom of patients to choose their doctor; otherwise, a practitioner not consulted by many people would have to be paid as much as one whose services are in constant demand. In the last analysis a salaried service could be efficiently run only along centralised lines. The danger which such a service would constitute to the professional freedom of doctors has already been mentioned.

FEE-FOR-SERVICE

The attraction of a fee-for-service system is that it would automatically rehabilitate general practice, simply by the working of economic laws. No subsidiary measures would be needed to ensure that N.H.S. practitioners would, after some years, practise active medicine once again. Some regulations would, of course, be required to curb abuses, and others might be desirable to assist the aims of a fee-for-service system.

Redirection of services, modernisation of equipment and surgeries, and acquisition of lost skills take time, and it would probably he necessary to introduce a fee-for-service system in two stages. In the first stage, which might have to last for about five years, a capitation fee of about half the present value would be retained, the rest of the practitioner's earnings being made up by fees for service. At the end of the first stage, lists should be abolished and payment should be made wholly by fees for service.

Fee-for-service Pool

The main objection to fee-for-service is that it invites abuses which are difficult to control and which would put the Exchequer to an unjustifiable and unpredictable expense. Therefore the remuneration of G.P.s should come out of a predetermined pool as at present. The size of the pool should be determined by an agreed average income per practitioner. This would leave it to the doctors to deal with abuses perpetrated within their ranks and to bear the brunt of such abuses. The size of the pool would increase only when new doctors open up practices. Since the object of a fee-for-service system is to recapture for general practice many of the activities which are now neglected or carried out by hospitals and clinics, there will be a tendency for the number of G.P.s to increase. This would be the natural and desired result

of a fee-for-service system, and the additional cost should be reflected in an increased efficiency of the service and in a corresponding absolute or relative shrinkage of expenditure for hospitals and clinics.

Certain hospital gains in establishment and facilities have become consolidated to an extent that they will not be returnable into general practice. The recovery of general practice will therefore undoubtedly be followed for some years by an increase in the absolute cost of the service to the nation. This represents no more than a natural expansion of a service which is as yet not fully adequate, and the deflection of this expansion into G.P. channels will be of ultimate benefit. From the retention of a pool it follows that fees would have to be calculated in units of some kind and would vary from time to time.

Whilst retention of the pool would rob fee-for-service of much of its potential financial danger to the nation, it would still be in the public interest to discourage abuses and to ensure a fair share-out. The upper limit to which the pool will be allowed to expand may eventually have to bear a relation to the number of patients treated.

Signature for Service

Abuses of any system of payment may be divided into those which are openly fraudulent and those which are insidious and within the law. Under a fee-for-service system the first category consists in claims, with or without the collusion of the patient, for services not in fact rendered. Where there is no collusion, the remedy is to obtain the patient's signature for every service rendered, a method which is used in the dental service. Where doctor and patient conspire to defraud the service we are dealing with a criminal act such as can be perpetrated in any organisation. Such crimes cannot constitute a valid argument for or against any system of payment and the remedy lies in appropriate penalties.

Over-itemisation

The insidious or quasi-innocent abuses of a fee-for-service system are of greater interest. Over-itemisation of pay claims is encouraged by a fee-for-item-of-service system which breaks up the doctor's work into unnatural units. To have scales of payment, evaluating such activities as the taking of blood-pressure or the giving of an intramuscular injection, is absurd and invites abuse. The remedy is obvious—namely, the avoidance of such scales. The list of services should be short and comprehensive and should prescribe fees for consultations at the surgery, for home visits, for minor operations, for antenatal care, for vaccinations, and so forth. It would probably be wise to launch a fee-for-service system with a few agreed items and to expand the list slowly and after full consideration at all levels, utilising whenever possible the experience of other countries.

Patient Contribution

Overtreatment is the real bugbear of a fee-for-service system, because its definition is largely a matter of opinion. If we wish general practice to re-expand into a living branch of medicine we must give the individual practitioner freedom of therapeutic judgment; on the other hand unopposed discretion in this respect could seriously endanger the health service. The only natural and acceptable brake on overtreatment is to make the patient pay a part of each fee charged.

Political objections to this proposal could be partly met by abolishing the present fee for prescriptions, but in order to make the patient's contribution economically effective it would, under present circumstances, have to be of the order of about half-a-crown. Special concessions would no doubt have to be made for underprivileged citizens of our Welfare State, such as old-age pensioners, who until the nation has learned to treat them decently might be allowed to remain capitation patients.

It will no doubt be objected that under such a system many people would neglect to go to the doctor even though they could afford it, simply from a disinclination to spend their money in this way. If they prefer to hang on to their money and their diseases, this privilege might be allowed them without endangering our free society. After all, the benefits of clinical medicine are more important to the individual than to society. Public-health measures (e.g., vaccination) might be exempt from contribution by the patient. Education and the need for insurance certificates will do the rest.

No doubt, the proposal of a contribution by the patient will excite great opposition, not only among the politicians but also among those doctors who have grown so delicate that they will accept people's money only when it comes to them via an official cheque. I am convinced, however, that a patient contribution is needed in a fee-for-service system to restrain a tendency to wholesale overtreatment. It would also in the long run produce a healthier and more realistic attitude to the health service by the people.

Anybody who thinks it possible to devise a medical service which is free from abuse by patients and doctors understands neither human nature nor the nature of medicine. Any fee-for-service system would be a hotbed of abuses. But at least it would allow good medicine to survive. With suitable safeguards it would present no drawbacks which would not far be outweighed by this tremendous advantage.

OTHER MEASURES TO ENCOURAGE GENERAL PRACTICE

Many cases are sent to hospital nowadays because the doctor feels that to treat them at home would impose unfair financial or social strains. To minimise these objections three measures should be enacted.

Hospital and home patients should be put on an equal financial basis. It was never envisaged that the N.H.S. should provide board and lodging in addition to medical care, but this is what hospital inpatients receive; they should either be charged for this, or patients confined to bed in their own homes should receive an equivalent allowance.

Secondly, there must be more complete nursing facilities for cases treated at home. A large proportion of the present inpatient population could and should be treated in their own homes. This would require more home nursing than is at present available. The corresponding relief of pressure on hospital beds would constitute an all-over saving.

Even if these two proposals were carried out, a great number of cases would remain where conditions make treatment at home impracticable but which fall medically within the province of the G.P. Such cases he should be able to admit to a local hospital *under his own supervision*. Next to fee-for-service, this one single measure would contribute most to the rehabilitation of general practice. It would at the same time reduce radically the need for medium hospital grades in non-teaching hospitals and would solve the registrar problem.

Nothing that I have proposed in this paper is meant to apply in any way to the medical schools and their teaching hospitals. The autonomy of these institutions is the very

foundation stone of medicine and must be preserved absolutely.

Prognosis

It is easy to fall into a trap but difficult to get out again. The measures which might rehabilitate British general practice are relatively simple and have been employed with success in other countries. Yet, very great determination would be needed to have them adopted. The politicians with whom the last word lies are prisoners of the thing they have created, and will not initiate unpopular changes in the structure of the N.H.S. except under irresistible pressure from the medical profession.

Who in the medical profession is likely to take up the cudgels on behalf of general practice? The leaders of the profession who regard the G.P. as something that has fallen off a ladder? The professors in their schools to whom the plight of G.P.s penetrates as a distant rumour, momentarily disturbing their efforts to balance out the electrolytes? The consultants, free at last from the importunities of the family doctors, secure from interference or scrutiny, doling out secret merit awards to each other? The senior registrars whose professional status is characterised by the fact that they have to write anonymous letters to the medical press? The registrars, hanging on for dear life, casting anxious glances at the multitude of old faithfuls above and of young hopefuls below? The housemen, expectant fathers before they have passed their finals, their eyes glued to the overseas columns of the medical journals? The B.M.A. which, having stampeded the profession into a service they did not want, is now spending its time in recoiling from its own harebrained schemes for getting out again? The general practitioners themselves, divided into those too old to care, too young to know, and a sizeable group who would look with considerable anxiety on the prospect of having to earn their living by positive skilled medical action?

I very much fear that the National Health Service is in for many years of steadily increasing dreariness and inefficiency.

Dialogues of Today

PUBLIC FACES

SOCRATES: Last night I was in the house of Apollodorus and he showed me on his teleoptic machine a distinguished doctor who was telling all who cared to look and listen about cancer; and today I gather from one of those who tell us what we ought and ought not to do that he was wrong to do this, and that he was offending against one of the rules of his profession. What do you think, Eryximachus?

ERYXIMACHUS: I too think he was wrong, Socrates; for it is a well-established tradition of medicine that doctors do not advertise themselves, and this principle has recently been reaffirmed by those in authority. Even if such a doctor is not mentioned by name, he is well known, and anyone who wishes to find out who he is has no difficulty in doing so. In fact some doctors are announced by name, and not only do doctors appear teleoptically, but they now write on medical matters for the general public in books and elsewhere, and our old ethical standards are being undermined, and with them, I fear, will go the dignity and status of our profession. If we behave like advertising agents we cannot complain if both the public and the Government treat us like advertising agents.

SOCRATES: You evidently feel strongly about it, Eryximachus. When you say the principle of which you speak has lately been reaffirmed by those in authority, you are alluding, I suppose, to the medical tribunal which sits in judgment on medical offenders.

ERYXIMACHUS: The tribunal, Socrates, from time to time reaffirms the principle, but it does nothing about the practice. For, regarding itself as a judicial body, it will not pronounce on any act of a doctor which is not made the subject of complaint to it. Either therefore no such complaint has been made to it about the doctors' teleoptical appearances, or it has not thought them serious enough to investigate in public. In either case an established practice has grown up unchecked which would now make it difficult for the tribunal to rebuke anyone who did no more than has been done by many well-known doctors for years. Leaders who do not lead are likely nowadays to be led by events.

ANALYTICUS: In my view, Socrates, the days have gone by when doctors could be regarded as a secret society keeping from the public knowledge which it had no right to know. Medical knowledge is no different from other knowledge: indeed it may concern people more closely than most. If the public wants to know about health and disease it has a right to do so and doctors have neither right nor reason to prevent it. I myself would bow to convention to the extent of appearing anonymously, but I think there is much force in the argument that people are entitled to know what the source of their information is, and will value it more if they do. Besides if a doctor is to speak about medicine to the public he should do so openly, so that his colleagues can criticise him.

ERYXIMACHUS: It seems to me, Socrates, that what Analyticus advocates is not free from danger. We all know how difficult it is to explain matters to our patients, and the layman may easily misunderstand something he hears in a talk from a doctor whom he cannot question, and get the idea that the speaker is giving him advice contrary to that which he has had from his own doctor.

SOCRATES: Tell me, Analyticus, who decides the subjects upon which the public is to receive broadcast information?

ANALYTICUS: The broadcasting authorities.

SOCRATES: And do they provide this information because it is what they think the public wants, or for some other reason?

ANALYTICUS: Because they think it will interest the public; but of course they have their medical advisers.

ERYXIMACHUS: Who are responsible to no-one but their employers.

SOCRATES: So what the public learns in this way about medicine is determined ultimately by public demand?

ANALYTICUS: That is so, but why not? The broadcasting authorities have no other interest.

ERYXIMACHUS: No other interest! Doesn't it strike you as ironical, Analyticus, that Socrates should have heard about the dangers of cancer from a doctor using a medium which earns a great deal of money by advertising what is known to be a cause of cancer? How can doctors accept that without an intellectual qualm, let alone a moral one? Besides, doctors who appear on the teleoptic are not chosen merely because they are experts in medicine, but because they are, or become, experts in that mode of publicity. Others as good or better, but lacking that art, are not chosen. Medicine is presented to the public by doctors who, however excellent, are unrepresentative. But I easily talk too much about this. Tell us, Socrates, what you think.

SOCRATES: I think you are both partly right. Analyticus is right when he says that there is a new public today whose need for information about medical matters should be met. Eryximachus is right in saying that there is much which is undesirable in the present state of affairs. That doctors should defy established conventions must make for dissension within the profession, and lower it in the esteem of those whose good opinion it should value. But if the convention needs review, that is the profession's own fault. If the tribunal can or will do nothing about it, let the chosen leaders of the profession consider the matter afresh. And if they agreed about an ethical code appropriate to the present day, most doctors, I am sure, would observe it, and if some did not it could easily be enforced.

In England Now

A Running Commentary by Peripatetic Correspondents

WHEN my wife went to hospital the other week for her fourth confinement, we noticed changes. Away had gone the rusty can from which quarts of soapy water eased its uncomfortable way down yards of tubing into the nether regions—now it is done with some kind of chemical squeezed gently from a sort of toothpaste tube. Jolly comfortable. It didn't work, of course, but it was jolly comfortable. The whole affair seems otherwise much the same mechanically. The baby still comes out head first and so on, but the accessories after the fact are different. The accent seems to be on doing as one pleases. Husbands are even allowed to visit at their convenience.

But the biggest surprise was at the end of the first week when the house-surgeon said things seemed O.K. all round and she might as well go home. I could not but recall for him a previous event when, with the same wife in the same department of the same hospital eight years ago, I had attempted to secure her discharge 48 hours before the statutory 14 days. The sky fell. The then houseman looked very solemn, and the senior registrar rang me that night saying how much he deplored it. Sister interviewed me coldly in her office reminding me that, however well my wife was, I should think of the bad effect it would have on the morale of all the other women. The entire staff from cleaners upwards regarded the three of us with thinly disguised hostility.

I daren't think what the reaction would have been this time if had I suggested keeping her for 48 hours over the 7th day. I would presumably be told pityingly that I was getting a bit old and past it—rightly perhaps. However, I can't help wondering whether we shan't be back to square one in a few years' time, when someone does statistics on prolapse or something. On the whole, perhaps domiciliary midwifery is the thing: one is less subject to the transient whim of fashion.

* * *

Peripatetics of today may be interested to see with what scant sympathy the patients of classical times regarded their physicians. The following is an inscription taken from the now famous Phosphatic Stone, upon which, like so many of the priceless fragments of knowledge we owe to the past, it was carved in a corrupt Greek dialect.

You ask me, Æsculapius, how I have lived so long
And what's the mystic secret keeps me applecheeked and strong.
Well, I wonder at your question and I marvel that your arts
Reveal to you so little of the secrets of men's hearts.
'Tis not because I diet, practise rituals, or fast
That I shall dance upon my doctor's tomb and mock him, at the last;
So hearken to the simple lore which keeps me ever young—
I can tell if I am right, but never know when I am wrong.

Some medical historians claim that the first psychosomatic theory was put forward in the classical dictum *Mens sana, vita brevis*. On the other hand it must certainly have been a patient, probably a private patient, who wrote *Quem deus vult perdere, prius medicatur*.

* * *

Psychiatric research among the shoals of obese children who throng our pædiatric clinics and permanently flatten the springs of the beds in the metabolic ward has led me to a great discovery. One of my fattest patients has proved to have a fantasy life of Gothick proportions and pattern. Here is a typical story which he recounted extempore when I invited him to describe a prosaic picture of a girl leaning on her broom.

Nurse was sweeping down the ward corridor, when she saw a marvellous man going past. Ooh! Really lovely! Blond hair and that sort of thing. She brushed accidentally against him with the broom, and that is how they met. She said "Hello". He said "Hello, that's a nice job you've got." She said "Oh I dunno, on your feet all day." They laughed. She could not sleep that night. They met day after day. On the third day he tripped over her broom and he fell on the floor. It was the day she was going to propose to him. But his trousers legs lifted up and he had two wooden legs, which knocked against his body and killed him. To this day she keeps a chip from his wooden leg in a glass case in her room.

I am still hard at work trying to correlate the story with his obesity. A really good children's psychiatrist should, I am sure, be able to wangle some sort of allegory out of it all. My non-psychiatric colleagues claim that all I have discovered is one novelist, very young and very fat.

* * *

Looking for tadpoles last week in our favourite loch the best we could find was a two-inch eel-like creature, apparently some kind of fish. In the jar on the way home it proved to have a most unfishlike capacity for attaching itself to the glass with its hinder end and waving the rest of its most extensible length about above water, and our dreadful suspicion that it must be a leech crystallised into certainty when it proved to be able to do the same thing with its front end as well. A most anxious debate began as to how we were to feed it. The most popular suggestion was that Daddy should be sacrificed to it weekly. Our pond-life book fortunately proved that it was a horse leech, and that despite its horrific name of *Hæmopsis sanguisuga* it does not suck blood, but lives on worms and snails. So we sacrifice a small worm to it every other day instead, and it seems to approve of this. Indeed, we are becoming most attached to it, and much prefer it to tadpoles. It has a most engaging manner of waving its front end about above water when it is hungry, just like a zoo sealion at feeding time: clearly the author of *Proverbs* with his tale of the daughters of the horse-leech crying, "Give, give, give" had watched one poking out of the biblical equivalent of a jam-jar. And Grand Guignol has nothing on its mode of swallowing a live worm slowly and then lying in a comfortably bloated attitude with the wriggling worm inside it making irregular bulges, like the abdomen of intestinal obstruction.

So fascinating is it that we suspect an ulterior motive in the popularity of the medicinal leech for so many years. Clearly it must have been the doctor's children's best-loved pet. When the pet was hungry, Daddy was sent out to find food for it: no worms for *Hirudo*, only the squire's plethoric blood was good enough. Mark Twain has a tale of a doctor who built a remedial gymnastic exerciser, by means of which he induced his patients unwittingly to pump his water up for him. Our fathers' manner of feeding their children's pets was probably even more subtle.

* * *

My peripatetic colleague who lately described his suspicions of poltergeist activity in his hot-water system (April 25) will be interested in the experience of my friend George, who has just had a new boiler fitted in his house. For the first three days he told us how excellently it worked, giving four hot baths every evening and scalding water for washing up. On the fourth day he was ecstatic; the fire had dwindled to a few small embers in the grate, and still the four hot baths were drawn. On the fifth day his face had changed; the fire, it seemed, had gone out completely but the water had remained as hot as ever. Investigation revealed no poltergeist, but an immersion heater left switched on by the plumbers.

* * *

In the Garden.—VIII

TERMINOLOGICAL EXACTITUDE

Professor Henry Artemus Swayback was a verbalist,
And also a herbalist.
That is, he grew herbs
And cultivated verbs.
All his plants were labelled with their Latin names
And even his dog Fido was only allowed to play dog-Latin games.
One day his wife said that his only daughter
Had done what she really didn't oughter;
She'd eaten Nightshade berries and was maybe a gonner.
He said "Not Nightshade, dear, Belladonna."

Letters to the Editor

EXPERIMENTAL UNIT FOR MENTALLY AND PHYSICALLY HANDICAPPED CHILDREN

SIR,—In view of greater flexibility of hospital admissions under the Mental Health Bill, it seems useful to discuss the needs of a borderland group of children—those with severe mental and physical handicaps. These are children so handicapped mentally that they require the type of training and education given in a mental-deficiency hospital, and are debarred from education in hospital schools under the Education Act; so handicapped physically that they require the full range of medical services available in a children's orthopædic hospital not usually available in a mental-deficiency institution. They tend to be so handicapped that they require long-term inpatient treatment.

Two such overlapping groups are (*a*) children with spina bifida associated with lumbosacral myelomeningocele, hydrocephalus, and mental defect; and (*b*) cerebral-palsied children with associated mental deficiency. We have been unable to find conclusive figures of the incidence of spina bifida with lumbosacral myelomeningocele and mental deficiency: there are figures [1–3] that suggest there are quite a number. We do know that the incidence of children with cerebral palsy is 1–2 in 1000, and that almost half of them would have I.Q.s below 70.[4]

No-one yet knows how much can be done for these children given (*a*) full clinical diagnosis followed by (*b*) treatment geared to their mental and physical handicaps. We quote 2 cases which suggest that such children may make a worthwhile, though limited, response to treatment:

CASE 1.—A spina bifida with paraplegia and arrested hydrocephalus, certified mentally defective, was bedridden and incontinent, with flexion deformities of hips and knees on admission at age 5. Now aged 12, she is ambulant (with crutches and callipers) and continent (after an "ileal bladder" operation), I.Q. 53 (borderline educable).

CASE 2.—A spastic quadriplegia, admitted at 14 months with extreme general retardation, certified mentally defective at age 8, I.Q. 48, and now awaiting transfer. But physiotherapy and corrective surgery have produced increasing mobilisation and he can now feed and wash himself.

We should like to suggest that an experimental unit for 15–20 young mentally and physically handicapped children could be set up in a children's orthopædic hospital, with occupation-centre or nursery-school staff to look after the social and educational side. Such a unit appears to have the following advantages over either a separate unit for these children or a unit attached to a mental-deficiency institution:

(1) Medically the children would receive the full range of expert services available to other children in the hospital suffering from the same physical disabilities. In spina bifida and cerebral palsy the physical disability cuts across the range of intelligence: therefore the hospital staff in a children's orthopædic hospital has experience and knowledge of the problems involved in physical habilitation of these conditions. A further point of some importance is that it may be easier to maintain a high level of staff morale where staff treat children of normal intelligence as well as mentally subnormal children.

(2) Educationally and socially the mentally retarded children would be provided for as a separate unit, distinct from the hospital school attended by the other children.

(3) There would be constant exchanges between hospital and teaching staff, and therefore this unit would be an integral part of the hospital. However, these children would not hold back the brighter children educationally and socially, and they would not have to compete with the other children in fields which they would find hardest—namely, in educational and social life.

(4) A last advantage would seem to be that in children with multiple handicaps accurate diagnosis is often difficult and needs time, and a unit such as this would allow for flexibility without major changes of personnel or environment.

Such a unit should be an experiment. Our argument is that it is worth while to get these children as fully independent as possible, because it will increase their happiness and self-respect: any degree of social independence lessens nursing care, and is therefore important economically. The object of the experiment would be to find out whether one can achieve a useful degree of independence with such a programme. The children would be carefully assessed initially and reassessed at intervals. It should be possible to obtain control groups from mental-deficiency institutions or occupation centres or outpatient departments.

E. P. QUIBELL
ELSPETH STEPHEN
ELIZABETH WHATLEY.

Chailey Heritage,
Chailey, Sussex.

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HOSPITAL DIET

SIR,—Your note of April 18 about the recent publication of a third memorandum on hospital diet is indeed timely. The memorandum is so excellent a document that it should receive the widest possible publicity for, were its recommendations to be fully implemented on a national scale, the standard of the hospital service would be immeasurably raised.

As you emphasise, it is generally recognised that good food, well cooked and attractively served, is an important factor in the treatment and recovery of every patient. A well-balanced normal diet, no less than a therapeutic diet, requires trained personnel, including qualified catering officers, cooks, and dietitians. The catering department is as important as any other of the hospital service and yet often, especially in the periphery, catering for normal diets is quite inadequate while facilities for therapeutic diets are virtually non-existent. Moreover, kitchen hygiene is not always above reproach.

Yet most hospitals, central or peripheral, can boast of, and indeed would not tolerate anything but, the best medical, surgical, or pharmaceutical services.

What then is the cause for this lower standard of the catering department? One of the answers lies in what Dr. Avery Jones, chairman of the Hospital Catering and Diet Committee, refers to in his foreword as the "structural inadequacy of kitchens in many hospitals which are not only poorly equipped but also badly designed". In fairness, however, one must agree that the Ministry of Health have readily accepted the principle that catering departments are of key importance—witness the great improvements in some of the major hospitals, especially during the past decade. Not, however, until hospital capital expenditure is increased so that new hospitals can be built will their kitchens become satisfactory and some of the antiquities of today become no more than a sordid memory.

The second most important problem to be solved is staff shortage. The national salary scales are far too low by comparison with current commercial levels to attract trained personnel, from catering officer down to kitchen assistant, not excluding the important dietitian whose role as therapist, teacher (to patients, nurses, and cooks), and nutritionist is so well outlined in the booklet. As a temporary measure to deal with the immediate problem, could not existing resources be pooled and administrators and hospital management committees consider more even distribution and sharing of catering personnel between two or more hospitals in a group rather than concentrating on the well-developed departments of some of the major hospitals? This would help to promote a general upgrading to an accepted standard of efficiency.

PHILIP ELLMAN.

London, W.1.

" AUTO-IMMUNITY "

SIR,—With reference to your leading article of Feb. 21, we write to support your implied criticism of the term " auto-immune " as descriptive of these conditions. We have been interested in this group of diseases for many years,[1–3] and some time ago we suggested that they should be called the auto-allergic hyperreactive diseases.[4] We consider that this term is more accurate than " auto-immune ". " Auto-allergic " means an altered reaction involving the hosts' own tissues. It expresses clearly a fundamental defect in these diseases, which is that the host has become allergic to one or more of his own tissues. The tendency to the development of auto-allergy is favoured by a hyperreactive state. Evidence of this is to be found in most of these cases and so " hyperreactive " was included in our definitive term.

We suggest, therefore, that " auto-allergic " should be used in preference to " auto-immune " as the descriptive adjective for these conditions, and we should be glad to hear of the reactions of others to this suggestion.

Poliomyelitis Research Foundation Laboratories, Johannesburg. J. H. S. GEAR Director of Research.

PRISON MEDICAL OFFICERS

SIR,—I should like to reply to some of the remarks by " Another Prison M.O." in your issue of May 2.

The American psychiatrist, H. S. Sullivan, has rightly said that any disturbance of interpersonal relationships is the concern of psychiatry. Most workers in the field of human behaviour, whether psychologists, neurophysiologists, psychiatrists, or psychoanalysts, are unanimous that there is no clear dividing line between the normal, neurotic, psychotic, or criminal personality. There is in all of us a mixture of these characteristics. Theologians call this original sin. A person's behaviour at any given moment is the result of the physical activity of his nervous system, and whether that behaviour is what we call " socially acceptable " or " unacceptable " (i.e., " criminal "), or whether it is neurotic or psychotic, is determined by the interaction of the anatomical and physiological equipment of a person's nervous system with the past and present stimuli that he has received from his total environment, including, if you wish, the stimuli he receives from God in the means of grace. Crime, therefore, is a psychological disease and is very much the concern of psychiatry.

I would remind your correspondent that one hundred years ago physicians were powerless to treat the majority of physical disease. Fortunately, however, they did not therefore conclude that because of their failures they should hand their cases over to the theologian or politician, as he advises psychiatrists to do in the case of delinquency. The future success in the treatment and prevention of crime, however far off, and however ineffectual it may be at the moment, lies in the hands of all who study human behaviour. Psychiatry will play an increasingly vital and effective role.

I would suggest that " Another Prison M.O. " is, or should be, responsible for the physical welfare and comfort of the prisoner. He needs to be a good general practitioner with a sound knowledge of public health which includes, indeed, the ability to understand and alleviate the day-to-day unhappiness and anxiety of his patients. In the latter context if the prison authorities allow him the opportunity, he has a very vital psychotherapeutic role to play.

The complex problem of responsibility for crime and the treatment of an offender is the province of the psychiatrist. One hopes that in the future criminal psychiatry will be a full-time specialty in its own right, just as child psychiatry is today. Much of the ineffectiveness of present psychiatric advice and treatment in the field of crime is not the fault of psychiatry itself, but rather that there is no opportunity for psychiatrists in training to receive any worthwhile experience or tuition in this field. So long as society is concerned with punishment and responsibility for sin, rather than concern for the understanding and treatment of disease, progress will be very slow.

Carlton Hayes Hospital, Narborough, near Leicester. H. B. KIDD.

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ULCERATIVE COLITIS AND CARCINOMA COLI

SIR,—We were interested to read the article by Dr. Rosenqvist and his colleagues (May 2). We have recently studied this problem in 663 patients with ulcerative colitis.

We found 19 cases of carcinoma (17 of these have been reported in summarised form,[1] and a full report has been submitted for publication).

Our findings support Dr. Rosenqvist's observations that carcinoma occurs in longstanding colitis at a relatively early age and has a poor prognosis. We differ from him, however, in certain important features.

9 of our cases (47%) developed carcinoma of the rectum, as opposed to 2 (8%) in his series. We also consider that in some of our cases pseudopolyps underwent transformation both to true polyps and to carcinoma. Dr. Rosenqvist suggests that of patients who have had ulcerative colitis for ten to twenty years, 1 in 3 will develop carcinoma of the large bowel. In our series, 127 patients have had colitis for more than fifteen years, but only 10% have developed carcinoma.

The Vincent Square Laboratories of Westminster Hospital, London, S.W.1. IAN M. P. DAWSON J. PRYSE-DAVIES.

ANTIBIOTIC COMBINATIONS

SIR,—Dr. Sales (May 9) claims that novobiocin should not be used routinely " because of frequent sensitivity reactions ". This antibiotic has been in general use for several years and the number of sensitivity reactions (at normally accepted dose levels) has been small. In a series of 208 cases the incidence of a drug rash was found to be less than 0·5%.[2]

The raison d'être of ' Albamycin-T ' is the provision of a combination of novobiocin and tetracycline to attempt to preserve the antibacterial efficacy of these two antibiotics. Evidence exists that a combination of two antibiotics is more effective than either singly and that, of a number of combinations, novobiocin and tetracycline was the most satisfactory in this respect.[3] Also, the effective use of a combination of novobiocin and erythromycin in a general hospital to lessen the danger of erythromycin-resistant staphylococci is proof that the use of antibiotic combinations is both useful and practicable.[4]

Whilst agreeing with Dr. Sales that a combination of two bactericidal antibiotics may be ideal, evidence at the present time suggests that a combination of novobiocin and tetracycline is particularly effective against staphylococci [2] and this combination provides a very wide spectrum of activity—almost all pathogenic organisms commonly encountered in general practice fall within its scope.

There are of course many occasions when the practitioner can be reasonably certain that a particular infection is caused by a particular organism and, on these occasions, the choice of the most suitable antibiotic is easily made. However, on the many occasions when the organism cannot be rapidly and accurately identified at the bedside or when a mixed infection is suspected it is reasonable to use a combination of antibiotics which can be expected to control the infection efficiently and rapidly.

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It is generally accepted that an increase in the number of strains of organisms resistant to the antibiotics at present available is one of the chief problems of antibiotic therapy. There is evidence that by using combinations of antibiotics this can be, at least partially, overcome and therefore the use of novobiocin and tetracycline for this purpose can hardly be described as "blunderbuss therapy". Further, it is difficult to understand what are the "disadvantages" that would be associated with this therapy: unwanted side-effects are less with the combination than with either antibiotic singly and resistant strains of organisms are less likely to develop.

A. R. H. HICKS
Crawley, Sussex. Medical Adviser, Upjohn of England Ltd.

FACTORY AND DOCTOR

SIR,—Life in general and medicine in particular is becoming more specialised. Any reasonably competent doctor can achieve most of the specialties if he has the requisite aptitudes and interests. General practice is quite rightly becoming recognised as a specialty in its own right and it is developing in the direction of epidemiology and preventive medicine.

To imply, as Lord Taylor and his supporters do, that industrial medicine can be made part of general practice, means either that industrial medicine is the purview of part-timers or that general practitioners need their afternoons filling and their boredom alleviated by a few works surgeries. Surely this attitude is unfair to both sides.

It is unfortunately true that much industrial medicine is little more than first-aid and rest-room treatment—but it should not be so.

The industrial medical officer is an environmentalist with a special interest in, and knowledge of, the problems of industry. Because he has this background he is a trusted part of the management-labour team. Similarly the doctor who has a special knowledge of the problems of the top executive is uniquely able to help them. Top executive examinations are not just "Life Insurance Guineas"—they are a valuable and specialised part of the industrial medical service for which particular skills and interest are required.

An atypical industrial medical organisation like Harlow (and it is worth noting that Slough is run on a full-time basis) may be able to work on part-time general practitioners, but in the main I am sure that both industrial medicine and general practice will best be served by developing along parallel, but independent, lines. To say that the practitioners of both, just because they have a common interest in preventive medicine, are the right people to take in each other's washing, is surely to oversimplify the problem.

London, W.9. H. BERIC WRIGHT.

PANIC AND PHOBIA

SIR,—The article by Dr. Nicolas Malleson (Jan. 31) and the correspondence that followed encourage us to report the following case.

A healthy woman, aged 38, was recently admitted for cauterisation of the cervix. Eight hours after this minor procedure, done under a general anæsthetic, she complained of nausea and vomiting. She was given an intramuscular injection of 25 mg. of chlorpromazine. Some four hours later, at 11.30 P.M., she was found dazed and hysterical wandering in the grounds of the hospital, having unlocked the back door of the ward.

She was examined and apart from her extreme apprehension and dismay because of her conduct and a slight graze over the right eye, nothing abnormal was noted. She was put back to bed and put on phenobarbitone gr. $^1/_2$ three times a day. The next morning her temperature was 100. By 10 that night her temperature was 104. We could find nothing to account for her temperature and by the following morning it was normal. Over the next 48 hours her temperature varied between 98·4 and 100, and for the final 3 days she was in hospital her temperature was normal.

While the temperature was elevated she was extremely agitated, not because of her experiences but because of the trouble she had caused other people and because she was very anxious that people should not think ill of her. She denied any similar walks at night, but her husband told us that she had done this twice before, on both occasions when she was pregnant. There is no history of mental instability, but it is perhaps of interest that her sister has schizophrenia.

The following pathological investigations were done on the morning following her temperature of 104. A white count showed a total of 4400 per c.mm. with a normal differential but complete absence of eosinophils. A high vaginal swab was normal. On examining a catheter specimen of urine there was no urinary infection but many granular casts were seen. In a catheter specimen of urine taken on the sixth day, however, there were no casts. An expert opinion was sought and we were told that a renal lesion could not account for her temperature, but that the temperature might explain the casts in the original catheter specimen of urine.

We believe that this is an example of a psychogenic fever.

ROSA HENDERSON
Pembury Hospital, Tunbridge Wells, Kent. ROBERT STEPHENSON.

SHAKESPEARE AND MEDICINE

SIR,—In your review last week of Mr. Simpson's book, you state that the only full-length study of the medical allusions in the plays appeared almost a hundred years ago. An article [1] entitled Shakespearian References to Disease and Medicine by R. C. Swan was published, however, as recently as 1957 in *The London Hospital Gazette*. While not, admittedly, "full-length", this study is a "systematic survey . . . with some new observations" and refers to *four* books devoted to the medical aspects of the plays.

The Library, The London Hospital Medical College, London, E.1. J. P. ENTRACT.

SPHINCTEROTOMY IN CHRONIC RELAPSING PANCREATITIS

SIR,—At a recent meeting of the Association of Surgeons of Great Britain and Ireland much was heard about sphincterotomy in the t[illegible]atment of chronic relapsing pancreatitis and allied co[illegible]tions.

I am sure in some cas[illegible]tricture does not occur strictly at the sphincter, but ra[illegible]r at the *papilla* within the duodenum. I described a [illegible]mber of cases in a paper at the combined meeting of the British and Canadian Medical Associations in Toronto in 1955.

When the papilla is inspected from within the duodenum it sometimes reveals a severe stenosis, the ostium of which will admit only the finest probe. If a large urethral sound or bougie is passed down the dilated common duct it passes through the main body of the sphincter and protrudes into the duodenum but *not* through the papilla, and has all the appearances of a diminutive penis with phimosis. The treatment for this "constrictive papillitis" is, to my mind, best done by a circumcision of the papilla, inserting a number of circumferential sutures.

The main part of the sphincter rather resembles a grid-iron incision, as the duct passes through the outer longitudinal and the inner circular muscle coats, although some spiral fibres do also come off and wrap round within the double layer of mucosa to form the papilla. No doubt, strictures do occur more proximally, but I think that the common usage of the term "sphincterotomy" rather overemphasises the pathology, which may often be at the papilla rather than the true sphincter. This condition of "constrictive papillitis" has more recently been described by Ward [2] of Vancouver.

Bath. C. PATRICK SAMES.

1. *Lond. Hosp. Gaz.* 1957, **60**, 40.
2. *West. J. Surg.* 1958, **66**, 104.

ADVERTISING INQUIRY COMMITTEE

SIR,—I should like to enlist the support of your readers for an investigation into the advertising of medical and paramedical products, which this committee has undertaken as one of its activities.

The committee came into being after a debate in the House of Commons in November, 1958; the reaction to this debate by members of the public, and in the Press, pointed to a considerable and widespread interest in the subject. The first meeting was held at the House on March 4, under the chairmanship of Sir Henry Turner, and it was then resolved that the committee should conduct a series of independent inquiries into all aspects of advertising. In the sphere of the maintenance of health, the aim of the inquiry is to assess the statements made by some advertisers, in the Press and on the television screen, about the remedial value of their products.

Two points made in the first progress report, submitted at the committee's second meeting on April 29, were:

(1) Some thirty drug preparations with a sedative action, and described as "tension-relieving" or "soothing", are available to the public without prescription, in any chemist's shop, as the law now stands. In some people at least, this ready access to sedative drugs may encourage a morbid dependence.

(2) There appear to be no reliable data on the extent of self-medication as a social problem in this country.

Advertising Inquiry Committee,
49, Cresswell Place,
London, S.W.10. DESMOND O'NEILL.

LEPTOSPIRA BALLUM IN SMALL RODENTS

SIR,—The failure to demonstrate *Leptospira ballum* antibodies in small rodents in Scotland despite the recovery of the organism from the kidneys of the same animals [1] confirms some findings in Georgia, U.S.A. While some of the information which follows has been published, the observation concerning the absence of *Lepto. ballum* antibodies in mice has not.

In 1954 and early 1955, *Lepto. ballum* was isolated from 69 field-dwelling house mice, *Mus. musculus* (Linnaeus); 2 roof rats, *Rattus rattus* (Linnaeus); 4 old field mice, *Peromyscus polionatus* (Wagner); and 2 cotton rats, *Sigmodon hispidus* (Soy and Ord).

These isolations were made from kidney suspensions inoculated with one tube each of Chang's semisolid medium with 10% rabbit serum; Chang's semisolid medium with 15% horse serum; Fletcher's semisolid medium with 10% rabbit serum; and Fletcher's semisolid medium with 15% horse serum.[2] After inoculation the tubes were incubated at 28 C for 30 days, and isolates were confirmed at the Leptospira Research Laboratory, Communicable Disease Center, Chamblee, Georgia.

Despite the fact that *Lepto. ballum* was isolated from house mice and field mice, no serum-antibodies by complement fixation or agglutination tests were demonstrable in our laboratory. Because of this, serial dilutions of *Lepto. ballum* cultures were inoculated subcutaneously into 100 white laboratory mice (*Mus. musculus domesticus* [CFW]) and subsequent cultures made and sera tested for leptospira antibodies. Again, when kidney tissue cultures were frequently positive, no demonstrable *Lepto. ballum* antibodies were found.

Other mammals seem to develop antibodies at least to the complement-fixing leptospiral antibodies [3] and most probably agglutinating antibodies, as attested by the literature on serological surveys. This is in agreement with similar observations by Dr. Broom and Dr. Coghland.

Communicable Disease Center,
Chamblee, Georgia. JOHN F. WINN.

1. Broom, J. C., Coghland, J. D. *Lancet*, 1958, ii, 1041.
2. McKeever, S., Gorman, G. W., Chapman, J. F., Galton, M. M., Powers, D. K. *Amer. J. trop. Med. Hyg.* 1958, **7**, 646.
3. McKeever, S., Schubert, J. H., Gorman, G. W., Grimes, R. D. *Amer. J. vet. Res.* 1959, **20**, 192.

PHÆOCHROMOCYTOMA IN PREGNANCY

SIR,—With reference to our article on this subject in your issue of April 18, it has been brought to our notice that one sentence of the history of case 2 could be misinterpreted. The perirenal air insufflation revealed a rounded opacity over the upper part of the left kidney (fig. 2), which was thought to be the normal gastric fundus.

It has been the intention to prove or disprove this by giving the patient some barium by mouth in order to locate the gastric fundus, but she developed acute pulmonary œdema on the following day For the sake of brevity in the article, we had to say that the shadow was regarded as normal even though further radiology might have disproved this.

MARJORIE BENNETT
GORDON MATHER.
Bristol.

THE CRANBROOK REPORT

SIR,—Professor Scott Russell (May 2) makes a very important point on the lack of discussion of this report. But the silence is due to the nature of the report rather than the complexity of the subject. Any report which mainly awaits "natural development" and "spontaneous evolution" cannot create a stir in either camp—of those who are satisfied with the status quo (indeed a small camp) and those who would introduce change. Local liaison committees will not bring about early improvements and the status quo becomes more organised and thereby more difficult to change. Masterly inactivity, of course, often produces a good baby, but till the diagnosis is made, it is really no answer to a situation which may in fact demand masterly intervention. But discussion of the report qua report will not solve the main problem. The Cranbrook Committee has laboured, but it has been very much a "trial labour". We must take stock again.

The demands of the patient on professional skills are very varied, and the existing facilities are very uneven and unevenly applied. But surely the maternity service is the least complex part of the National Health Service. It serves largely a healthy population whose demands fall into easily defined categories. And is there any other branch of medicine which is so rich in available statistics lending itself to diagnosis of the whole problem? It is probably the easiest aspect of the National Health Service to tackle scientifically. In short, the problem really is simple: how to organise adequate "cover" without wasting expensive and sometimes thinly spread resources; and how to use professional competence and avoid overlap while ensuring that there are no gaps?

The extent of the problem may be clarified by examining the following aspects:

(1) Logistics of a maternity service—i.e., the factual data on which there is much agreement: what is adequate antenatal care, what facilities are required by those practising the various items, and their availability.

(2) The problem of application—"squaring" existing organisations and vested interests, which range from sheer inertia to more direct financial involvement. (*The Doctor's Dilemma* is still very much amongst us, though in a different degree.) Those who deny that this financial aspect has any influence in determining organisation, I refer to the Cohen Committee's report on general practice in the N.H.S. (para 69) (Practical Difficulties in the Establishment of Health Centres).

Professor Scott Russell may be right in saying that we are not yet ready for a unified service, but it is largely non-professional considerations that block the advances. Our financial interests are so arranged that cooperation is discouraged. (On the introduction of the N.H.S. there was a sudden access of hostility to the local-authority welfare services which were seen to be taking the bread

from the mouths of the G.P.) For example, if there is to be further cooperation between G.P.s, there is encroachment on each other's economics; would the consultants be prepared to encourage non-hospital units (under the care of general-practitioner obstetricians?) and so relieve the hospitals of the vast numbers of "normals" who are taking up valuable beds on social grounds?

It is the economics of the doctors and not the intrinsic difficulty of organisation which is the main bar to a better maternity service.

Birmingham. BERNARD BARNETT.

PRE-PACKED STERILE DRESSING UNITS

SIR,—We should like to record our experiences over the past six months with pre-packed sterile surgical dressings. These are prepared for us by a surgical-dressing firm as packed sterile units ready for issue to the wards.

Apart from the manufacturer's own tests, each batch is subject to control in our own laboratory by the inclusion in each batch passed through the supplier's autoclave of *Bacillus stearothermophilus* spore control tubes, and batches are held in store until the laboratory sterility test is reported satisfactory. Each dressing unit is individually double-wrapped and sealed for sterilisation, and, as an additional indicator, a 'Klintex' strip is attached to each twelve units package by the manufacturer prior to sterilisation. Bulk-packed units are sealed in a polyethylene bag and packed in a cardboard outer container for despatch to us.

Contrary to the suggestion in the M.R.C. report,[1] only a small variety of packs seems to be required to cover the bulk of ward dressings and we use only four types of pack. Further, an actual saving is made on the cost of the units supplied to us as compared with the use of conventional bulk-dressing materials. There is a considerable saving of nursing time in cutting dressings and packing drums, and, in consequence, the units are very popular. Trials have been carried out with packed sterile disposable dressing towels and it is hoped soon to extend the system to include these.

These observations may interest those hospitals where a central sterilising service may be contemplated, for we feel that this service from commercial sources could form the nucleus of such a service with considerable financial saving.

D. B. RICHARDS
J. H. HUMPHRIES
C. H. N. BENNETT.

Group Pathology Laboratory and Pharmaceutical Department, Neath General Hospital, Glamorgan.

FUNCTION OF THE TEMPORAL LOBES

SIR,—Referring to your annotation of Feb. 28, I should like to comment on the view that the temporal regions of the brain play an important if not exclusive part in the organisation of conscious behaviour. I should also like to take issue with the notion that a unified cerebral mechanism exists, involving parts of the hypothalamus, the temporal lobes, and the medial frontal cortex, and excluding the remainder of the cerebral hemispheres.

Careful study of brain anatomy and function has gone on for less than a century, and in that time hypotheses as to the mechanism of consciousness have continually shifted from holistic to mosaic ones—i.e., from concepts about the overall generalised capacity of the brain to those relating specific functions to specific locations. Those who stress the significance of the temporal lobes and minimise the frontal-lobe areas or other parts of the cerebral hemispheres are guilty of the errors inherent in a mosaic conceptualisation.

Recently, reports by Prof. H. G. Wolff and his collaborators at Cornell University Medical College have suggested that the highest integrative functions of man, such as the expression of needs, drives, and motivations, adaptive capacity, goal achievement, and the capacities to cope appropriately and effectively with life situations are independent of brain site. Deficiencies in these capacities are proportional to the quantity of cerebral-hemisphere tissue that is damaged, diseased, or missing. With increasing loss of cerebral-hemisphere substance they have found that these highest integrative functions have been progressively impaired, irrespective of the site of the loss. Thus, after occipital lobectomy many changes observed also in those having incomplete frontal resections were noted, including such behavioural changes as "altered reactions to painful stimuli, hyperactivity, cyclic fluctuations of mood and activity and irritability".[1]

Working at Cornell University last year, Dr. Loring Chapman and I observed a consistent relationship between degree of cortical atrophy (based on pneumoencephalographic data) and performance on conditioned-reflex procedures. Subjects with increasing generalised cortical atrophy took increasingly longer times and more trials (1) to establish conditioned responses, (2) to extinguish conditioned responses, and (3) to give up the task when responses were no longer successful—in a period of induced failure or frustration. Moreover, there was a striking correlation between performance in the laboratory and impairment of life functions, as noted above. What is relevant here in regard to your annotation is the fact that ventricular dilatation, which was used as an index of cerebral atrophy, was in all instances studied symmetrical, suggesting that atrophy was diffuse and not localised to one area of the brain.

State University College of Medicine, Kings County Hospital, Brooklyn, New York. ARI KIEV.

BLOOD-VOLUME IN CHRONIC NUTRITIONAL ANÆMIA

SIR,—The results in my paper of April 18 were obtained by single observations on patients with varying degrees of anæmia. Another approach is to make serial studies on individual patients as they respond to appropriate treatment and regenerate hæmoglobin.

14 similar patients suffering from iron-deficiency and/or megaloblastic anæmia have been studied in this manner by following the changes in their plasma-volume, &c., at weekly intervals for three to five weeks until their discharge from hospital. The results were:

BLOOD CHANGES DURING TREATMENT

—	Mean	S.E. ±	Range
Initial total hæmoglobin (g.)	94	9	50–170
Initial plasma-volume (ml.)	2500	115	1715–3320
Initial blood-volume (ml.)	2795	140	1870–3870
Final total hæmoglobin (g.)	365	30	210–535
Final plasma-volume (ml.)	2355	150	1775–3615
Final blood-volume (ml.)	3505	235	2470–5250
Maximum difference in estimations of plasma volume in individuals (ml.)	465	65	150–830

There was no demonstrable difference in the plasma-volumes before and after treatment, but the blood-volumes had risen markedly. In this short period of observation the mean hæmoglobin level had increased four times, but had not yet reached normal. The maximum differences in plasma-volumes found by the weekly determinations in each patient were quite high (150–830 ml.) and must be compounded of true variations and technical errors; how much of each remains unknown.

For normal clinical practice, and even for most research work, the measurement of the hæmoglobin concentration remains quite adequate as an estimate of the degree of anæmia.

Institute for Medical Research, Kuala Lumpur. P. W. G. TASKER.

1. *Lancet*, 1959, i, 425.

1. See Chapman, L., et al. Highest Integrative Functions in Man During Stress: The Brain and Human Behavior. *Proc. Ass. Res. nerv. ment. Dis.* 1958, **36**, 491.

BACK PAIN AFTER INTRAVENOUS VITAMIN K

SIR,—Lower back pain can complicate the administration of intravenous preparations of iron if given too rapidly. It may be associated with a syncopal attack, rigors, pyrexia, and headache, and was thought to be due to multiple capillary emboli in internal organs.[1] A fatal case was described, however, in which postmortem examination showed no evidence of emboli.[2] Goodman and Gilman [3] suggested that these toxic effects were probably due to free iron circulating in an unbound toxic form.

A case is described here in which a similar pain was produced by intravenous vitamin K (' Synkavit ').

A man, aged 63, with liver failure, was admitted after hæmatemesis. His prothrombin concentration was 58%, and he was therefore given 100 mg. of vitamin K in 2 ml. intravenously over a period of about 2 minutes. 2 minutes later he complained of severe pain in the lower lumbar region, accompanied by nausea, which lasted for 5 minutes and then disappeared. Next day a second intravenous injection of 100 mg. of vitamin K was given with the same result, and again on a third occasion. No hæmaturia followed these injections.

An intravenous injection of 2 ml. of physiological saline produced no pain, neither did 10 mg. of vitamin K nor 10 mg. of vitamin K_1.

It seems that the pain was produced by the rapid administration of concentrated vitamin-K solution. A dilute solution did not cause any unpleasant side-effects. The distribution of the pain and its severity resemble those produced by intravenous iron. The mechanism is unknown.

Middlesex Hospital,
London, W.1. PAUL TURNER.

MITRAL VALVOTOMY IN THE YOUNG

SIR,—The problems raised by the histological findings in auricular-appendage biopsies from mitral-valvotomy cases are not solved by Dr. Wagner's letter of Feb. 14. Leaving aside the question of " activity " for the moment, there is still the problem of why such a high proportion of operation specimens contain inflammatory lesions similar to those of rheumatic carditis (up to 75% in some series), whereas only a small proportion (15–25% in most series) of necropsy cases of rheumatic heart-disease contain similar lesions where death does not occur in an acute attack of rheumatic fever. When death takes place during an acute attack, the incidence of these types of lesion is high in the left auricular appendage.[4]

Dr. Wagner raises several possible explanations for this difference, including the one that necropsy material is not representative of the rheumatic process. This he claims to have disproved by an examination of a large number of biopsy specimens, but this could be answered only by a comparative necropsy and biopsy study. I submit that this explanation is probably the correct one. The cases coming to necropsy differ from those undergoing valvotomy—e.g., in age-distribution, the proportions in congestive cardiac failure, and the proportions with auricular fibrillation. It is almost impossible to get a large enough series of necropsy cases comparable to the valvotomy cases.

With regard to " activity ", the important question is whether or not progressive damage to the heart can be caused by the development and healing of rheumatic lesions in the absence of clinical rheumatic fever. If it can be shown in biopsy specimens that the earliest forms of rheumatic lesions can be found in the absence of clinical rheumatic fever, this would constitute very strong evidence for the view that rheumatic carditis can be subclinical.

While I do not accept Dr. Wagner's definition of " activity " or his histological criteria for " active " lesions (in this context " early " lesions would be preferable), I agree that early rheumatic lesions occur in biopsy specimens. It is most unlikely that this discrepancy between the presence of early lesions and the absence of clinical evidence of rheumatic fever can be explained by the effects of therapy (steroids or antibiotics) as suggested by Dr. Wagner and his colleagues.[5] A large proportion of patients with mitral stenosis have no history of an acute attack of rheumatic fever and none of them in my own series has had steroid therapy or prolonged antibiotics.[6]

It appears from my own and other observations that lesions in all stages of development are found in biopsies, as one would expect in a subclinical disease of considerable frequency. The disease eventually becomes quiescent or recurrences less frequent, death resulting usually from the damage inflicted on the heart by repeated episodes of subclinical rheumatic carditis and occasional attacks of acute rheumatic fever.

Departments of Pathology,
Universities of Birmingham
and Illinois. ROBERT LANNIGAN.

PSYCHOANALYTICAL TREATMENT

SIR,—With reference to Dr. Lee's letter of April 11, if a general practitioner in central London thinks that a patient needs analysis or psychotherapy, and the patient is prepared to pay at the rate of one guinea an hour with the same psychotherapist each time, it can be done. The psychotherapy clinic administered by The Open Way charitable trust is at present treating 50 patients who earn less—some of them considerably less—than £1000 per annum.

The Open Way,
7, Queen Anne Street, London, W.1. M. R. DUNWELL
Secretary.

Parliament

Mental Health Bill Reconsidered

AT the third reading on May 6, Mr. DEREK WALKER-SMITH, the Minister of Health, said that the Bill replaced the complex mosaic of the old law with a single comprehensive design, simpler to understand and in keeping with contemporary social and medical advances. Since it sought to balance three main considerations, which could sometimes be in conflict—the therapy of the patient, the liberty of the subject, and the protection of the community—much of the discussion in committee had centred on these issues. The associated subjects of the definition of mental disorder and compulsory admission to hospital had also been closely scrutinised. The discussions on the definitions had not led to any basic amendment, although there had been two useful clarifying amendments.

There had been more alteration to clauses 25, 26, and 29, which prescribed the conditions for compulsory admission. Clause 25, which dealt with admission for observation, had been amended to make clear that observation might be accompanied by other forms of medical treatment. Clause 29 had been amended so as to limit the emergency procedure, and a patient admitted on an emergency application could not now be detained for more than twenty-eight days unless an application for admission under clause 26 was subsequently made.

Improvements had been made in the renewal and discharge procedures. The intervals at which the authority for detention in hospital or guardianship lapsed if not renewed, giving the patient a right to apply to the tribunal, had been reduced for long-term patients. The maximum period would be two years, as against three years in the Bill as originally drafted and as compared with five years under the present law. Patients would thus be able to apply to the tribunal within six months, and, if

1. Nissim, J. A., Robson, J. M. *Lancet*, 1949, ii, 686.
2. Barritt, D. W., Swain, G. C. *Brit. med. J.* 1953, i, 379.
3. Goodman, L. S., Gilman, A. The Pharmacological Basis of Therapeutics. New York, 1955.
4. Thomas, W. A., Averill, J. H., Castelman, B., Bland, E. F. *New Engl. J. Med.* 1953, **249**, 761.
5. Tedeschi, C. G., Wagner, B. M., Pani, K. C. *Arch. Path.* 1955, **60**, 408.
6. Lannigan, R. *J. Path. Bact.* 1959, **77**, 49.

they remained so long, at the end of the first, second, fourth, and sixth years and at subsequent intervals of two years. Another amendment allowed patients to choose when to apply to the tribunal during these periods instead of being obliged to apply immediately after any renewal or else lose their right to apply.

Another important addition to the Bill was a new provision in clause 65 which permitted patients who were subject to restriction on discharge to require the Home Secretary to take the advice of the tribunal on their fitness for discharge at the end of the first year in hospital, and subsequently at the intervals at which they would be entitled to apply to the tribunal if they were not subject to a restriction order. The first schedule had been amended to ensure that, in addition to a doctor and a lawyer, the tribunal which heard applications would always include a lay member with suitable experience. In the difficult and delicate matter of who should exercise the rights of the nearest relative to object to compulsory admission and to order the patient's discharge, the basic test of kinship had been retained, but greater scope was given for applying the tests of fitness for the function and affection for the patient.

At earlier stages discussion had centred on whether the Bill should put a mandatory duty on the local health authorities in respect of their mental-health services. Mr. Walker-Smith said that he had devised a method whereby the authorities would be placed under a duty, but in a more flexible way, which allowed for local needs and differences of local circumstance. He proposed to issue a direction under section 28 of the National Health Service Act soon after the Royal Assent was given to the Bill, so as to impose a duty on local health authorities to provide these mental-health services. As soon as possible after that, he would issue a direction under section 20 of the Act requiring the submission within a period of, say, six months of revised proposals. The circular which contained this second direction would probably give detailed suggestions in the form of a model scheme. He had already sent out a circular to local health authorities and a hospital memorandum drawing attention to the recommendation of the Royal Commission that there should be a reorientation of the mental health services away from institutional care under the hospital service towards care in the community. Progress in mental health depended, among other things, on skilled people and research. The Medical Research Council had decided to set up two new committees: one on clinical psychiatry, under the chairmanship of Sir George Pickering, to advise it generally; and the other on the epidemiology of mental disorders, under the chairmanship of Prof. A. J. Lewis, to establish a more precise definition of the various mental disorders and to provide the basis for a realistic evaluation of methods of treatment.

Dr. EDITH SUMMERSKILL in welcoming the Bill emphasised that its real implementation would be found in the successful integration of community care, the hospital population, the general practitioner, and the local-authority service. She feared that some local authorities might drag their feet, not through indifference, but because of lack of funds.

Dr. A. D. D. BROUGHTON still regretted that the Bill removed responsibility for the incarceration of patients from the hands of the civil authority and thrust it into the hands of the medical profession.

Dr. REGINALD BENNETT praised the Bill for having bravely provided a definition of a psychopath, but he doubted if we were any better placed to help these patients. He hoped that the Minister would consider as early as possible setting up suitable institutions for them. In his view the Bill had lost a genuine opportunity by making no provision for the detention of psychopaths over 25.

Mr. CHRISTOPHER MAYHEW reminded the Members that, despite the Bill, problems such as overcrowding remained. He feared that there must be thousands of patients who would trade whole clauses of the Bill for a little more space between their beds. Now we must tackle shortages of space, staff, and research.

Mr. RICHARD THOMPSON, parliamentary secretary to the Ministry of Health, speaking at the end of the debate, said that as soon as possible after the Royal Assent the Minister intended to make an order repealing the provisions of the present Lunacy Act which prevented designated mental hospitals and registered hospitals and licensed houses from receiving patients informally without powers of detention and without the signature of a voluntary application form. This would allow the informal admission of patients to mental hospitals—and decertification of any existing patients who could suitably remain on an informal basis—to start at once without waiting for the longer preparations for repealing the whole of the existing Acts. The implementation of the other main provisions of the Bill would need a good deal of preparatory work, but the Ministry would get on with it as fast as possible and hoped to achieve an early result. A simplified layman's version of the Bill was being prepared. It might have to await certain parts of the Bill becoming law, but the Ministry were giving advice and cooperation to the National Association for Mental Health and he thought that they should get a fairly speedy result.

Smoking by Children

IN an adjournment debate Mr. FRANCIS NOEL-BAKER urged the Government to launch, without delay, a vigorous campaign to discourage smoking by young people and to prevent their being encouraged to do so by the business interests concerned. The attention of the British public was first drawn to the dangers of cigarette smoking by a report published in 1950, but nearly seven years went by before the Government accepted a special report from the Medical Research Council to the same effect. During that period it was estimated that over 100,000 people died from lung cancer in England and Wales, and no effective action was taken by the Government during that period.

Advertising of cigarettes and tobacco ought to be prohibited at once, if necessary by legislation, as has been done in other countries—in 1956 in Sweden, for example. Action should include a ban on slot machines, the ending of the cheap cigarette and tobacco ration to young Servicemen, an effective Government campaign designed specifically to dissuade young people from smoking, using all the techniques of modern advertising and the mass media, and more vigorous action to counter advertising by the tobacco interests.

Mr. RICHARD THOMPSON, parliamentary secretary to the Ministry of Health, said that the Government's attitude had been consistent. They took the view that the facts on the likely connection between cigarette smoking and lung cancer must be brought effectively to public notice so that all should know the possible risks. Of the local authorities circulated, 90% accepted the need for a publicity campaign to bring to public notice these risks. They mostly concentrated on children and young persons. They used the local Press, posters, pamphlets, films, lectures, discussion groups, family visiting, and other forms of personal contact.

The general assessment of the public reaction was interesting. Local authorities came to the conclusion that there was much apathy, and suggestions were being studied for further action, many not the responsibility of the health department.

Town-bred Pigeons

Viscount MONSELL asked Her Majesty's Government whether, in view of the report of the World Health Organisation that town-bred pigeons were generally diseased and could fatally infect human beings, they would curb the mass breeding of these pests on their property (notably on the back of the War Office) which for years had made large parts of Westminster dirty, dangerous, and insanitary and most of the seats in the parks unfit to sit upon.—Earl St. ALDWYN replied: Her Majesty's Government are advised that the risk to the public from infection transmitted by pigeons is so slight as not to constitute a health problem. Nevertheless, the mess made by pigeons in Westminster and elsewhere can be very unpleasant. All practical action is taken to discourage them from

breeding and roosting on the War Office building and other Government properties. The seats in the Royal Parks are regularly cleaned.

Obituary

ALBERT IRVING SHEPHEARD-WALWYN

M.D. Edin., F.R.C.P.E.

Dr. Shepheard-Walwyn, consulting physician to the Cumberland Infirmary, Carlisle, died on April 5.

He was born at Windermere in 1881 and was educated at Rugby. After graduating M.B. from the University of Edinburgh in 1905, he held resident appointments at the Edinburgh Royal Infirmary and was house-physician to George Gibson. Later he studied under Sir John Parkinson in London. From these two men he acquired a special interest in cardiology. Soon afterwards he settled in Carlisle. In 1926 he was elected F.R.C.P.E. He retired from his hospital appointments in 1946.

Two of his colleagues on the staff of the Cumberland Infirmary, J. N. J. H. and J. A. R., write:

"Shepheard-Walwyn had outstanding qualities as a medical consultant. His examination of a patient was meticulous and comprehensive; he kept pace with advances in medicine and made use of laboratory techniques as soon as their value was established. He had a high sense of medical responsibility and spared no time or effort when presented with a clinical problem. His long and wide experience gave him an uncanny intuitive faculty in diagnosis, but his final opinions were invariably based on a careful and logical consideration of all the data—and how wise these opinions were.

"He came of a musical family and was himself a skilled pianist, and other hobbies were photography and gardening. But some of our happiest memories of him are of the occasional stolen day spent with him and his spaniels walking up partridge in the turnip field, or shooting driven grouse on the Pennines, or fishing on the Eden. He rarely travelled abroad, and for holidays sped immediately north to the Scottish lochs and rivers. After retiring, and especially when he became less vigorous, Loch Awe was his favourite retreat, and he and a number of his friends usually forgathered there in spring and autumn. He kept a boyish spirit to the end, and those who shared these holidays will long remember fishing on the loch, picnics on its shores and islands, and happy evenings spent by a log fire."

Dr. Shepheard-Walwyn leaves a widow and two sons.

Appointments

BRYAN, MARJORIE G., M.B. Lond., B.SC. Wales, D.OBST.: senior assistant M.O. (maternity and child welfare), Wolverhampton.
DARLOW, A. R., M.B. Lond., D.C.H., D.T.M. & H., D.P.H.: assistant M.O., Hertfordshire County Council (Hitchin and Stevenage New Town area).
DUNN, M. J., M.B. Brist.: assistant M.O./school M.O., North Devon area.
JENKINSON, JANE G., M.B. Lond., D.C.H.: house-physician, The Hospital for Sick Children, Great Ormond Street, London.
MAITLAND, D. R., M.B. Edin., F.R.C.P.E., D.M.R.: consultant radiologist, County of Fife hospitals.
PICKUP, D. S., M.B. Lond., D.P.H.: assistant M.O., Halifax.
STEPHEN, J. L., CH.M. Aberd., F.R.C.S.E.: part-time consultant in charge of varicose veins clinic, St. Mary's Hospital, London.

Manchester Regional Hospital Board:

DENMARK, J. C., M.B. Lpool, D.P.M.: assistant psychiatrist (S.H.M.O.), Lancaster Moor Hospital.
MARTIN, R. H., M.B. Lpool, F.R.C.S.E., M.R.C.O.G.: consultant obstetrician/gynæcologist, South Manchester hospitals.
MOIR, C. C., M.B. Edin.: assistant pathologist (S.H.M.O.), Preston and Chorley Hospitals.
PUGMIRE, S. L., L.R.C.P.I.: assistant psychiatrist (S.H.M.O.), Whittingham Hospital, near Preston.
WILDING, A. ST.J., M.B. Edin.: assistant pathologist (S.H.M.O.), Ashton, Hyde, and Glossop hospitals.

Births, Marriages, and Deaths

BIRTH

BROWNE.—On May 5, to Dr. Muriel James, wife of Dr. I. Warren Browne, of Chichester and Bognor Regis—a son.

Notes and News

DEVELOPMENTS IN THE HOSPITAL SERVICE

Mr. Richard Thompson, parliamentary secretary to the Ministry of Health, addressing the Hospital Savings Association in London on May 7 said that at any time there are nearly half a million hospital inpatients in England and Wales. Well over $3^1/_2$ million people spend some time in hospital in the course of a year. Nearly 40 million visits are paid to outpatient departments every year, and it is remarkable that so many people can be treated with the absolute minimum of complaint.

In the first ten years of the National Health Service the Government has spent £100 million on hospital building, and expenditure has steadily increased since 1956: in 1958 it was £20 million, in 1959 £22 million, and in 1960 it is planned to spend £$25^1/_2$ million. In addition to extensions and improvements to old hospitals there are 14 new hospitals in various stages of construction, 5 partly completed and already in use.

Delays for patients on waiting-lists are shorter, despite the fact that many more patients are being treated. In 1949 there were 498,000 on the waiting-list for inpatients; at the end of 1958 there were 442,000. The number of patients has increased by more than 30%, while beds have gone up by only 6%. More efficient use is being made of beds by reducing the time they are empty, and by treating more people as outpatients.

Nearly a million more outpatients are being treated today than in 1949.

Over 40% of hospital beds are occupied by the mentally ill, and nearly one-third of the money available for hospital capital development is being spent on improvements in mental hospitals. The effects of the Mental Health Bill should lighten the load on mental hospitals by relieving them of many patients who could better be looked after in the community, either at home or in hostels. The Ministry is trying to break down the barrier between mental and physical sickness and to encourage people to take treatment on an informal basis as outpatients and at day hospitals.

Referring to the work of the Hospital Savings Association, Mr. Thompson said that it is a matter for pride in the hospital service that the administration of about 3000 hospitals throughout the country is largely in the hands of voluntary workers; in the Ministry's view this kept the Health Service both human and personal.

CHEMICAL BASIS OF BLOOD-GROUP SPECIFICITY

IN his Croonian lecture to the Royal Society on May 7, Prof. W. T. J. MORGAN, F.R.S., said that the discovery of the blood-group characters by Karl Landsteiner resulted in an early and striking division of human beings into sharply differentiated groups. These special serological properties of the erythrocytes and secretions do not vary during life and the substances giving rise to the specificity are inherited according to Mendelian laws and are excellent examples of the products of the activity of genes. A study of the properties and chemical structure of these specific materials makes a direct contribution to the rapidly developing subject of human biochemical genetics.

The specific substances are mucopolysaccharides—i.e., macromolecular complexes built up from carbohydrate units and aminoacids joined together by primary chemical bonds. It is difficult to establish that the isolated mucopolysaccharides are completely free from contamination with similar but non-specific materials present in the original native secretions or tissue extracts. However, strong evidence for the absence of such heterogeneity is essential if any significance is to be attached to the subsequent isolation of small amounts only of a particular oligosaccharide, aminoacid, or peptide. Specific substances, apparently homogenous on the basis of physical, chemical, and serological measurements, all contain the same four sugars—L-fucose, D-galactose, *N*-acetylglucosamine, and *N*-acetylgalactosamine—and at least eleven aminoacids.

The results of (a) partial acid and alkaline hydrolysis and (b) specific inhibition tests, using agglutinins, precipitins, and enzymes, give evidence for concluding that blood-group specificity is associated with the carbohydrate part of the mucopolysaccharide molecules. Thus, A specificity is thought to be associated with structures identical with, or closely similar to, the non-reducing end unit O-α-D-*N*-acetylgalactosaminoyl- (1→3)-D-galactosyl-, B specificity with O-α-D-galactosyl- units, H specificity with α-L-fucosyl- residues, and Le^a specificity with a trisaccharide structure containing non-reducing α-L-fucosyl- and β-O-D- galactosyl- units joined to *N*-acetylglucosaminoyl residues by (1→4) and (1→3) linkages respectively.

The fact that the group substances possess a characteristic immunological specificity, which is gene-controlled and which sharply differentiates one type of mucopolysaccharide from another, establishes these materials as chromosome " markers " of outstanding value, and they can be used to study the possibility of gene interaction. For example, the secretions of a " secretor " person of group AB can be shown to contain mucopolysaccharide molecules each of which contain both A and B specificity and not, as might be anticipated, a mixture of mucopolysaccharides some of which possess A specificity and others B specificity. In this instance, therefore, the product of the activity of the genes A and B is a new kind of substance in which two immunologically active groups coexist on a single mucopolysaccharide molecule.

On the basis of the biochemical and serological data, it is possible to suggest pathways for the biosynthesis of the blood-group specific mucopolysaccharides which accord well with the latest genetic ideas and account for the multiple group specificity found to be associated with native secretions and the purified mucopolysaccharide isolated from them.

NUTRITION IN AFRICA

A SEMINAR on nutrition problems in Africa is to be held from May 18 to 29 at Lwiro in the Belgian Congo. It is organised jointly by the Belgian Government, the World Health Organisation (W.H.O.), the United Nations Food and Agriculture Organisation (F.A.O.), and the Commission for Technical Cooperation in Africa South of the Sahara (C.C.T.A.)

In 1949 C.C.T.A. held the first African conference on nutrition, and since then there have been several courses, attended by a hundred or so participants. These workers, who include doctors, social workers, and agriculturists, have been studying the nutritional status of African populations, in particular their supplies and actual intake of food. Besides instructing the people in the type of diet needed for health and undertaking research into native agriculture, they have also established supplementary feeding programmes in the areas where diet was inadequate or deficient.

STERILISING AUTOCLAVES

THE need for cooperation between the professions was stressed at a symposium on the Operation of Sterilising Autoclaves held at Brighton Technical College on May 9. The meeting, organised by the School of Pharmacy, was attended by over 200 pharmacists, bacteriologists, engineers, nurses, and others from hospitals, industry, and universities throughout the country.

Dr. R. H. MAXWELL SAVAGE said that the physical and bacteriological considerations which determined sterilisation were relatively simple, and the necessary scientific knowledge had mostly been available for many years. What was needed now was partly a matter of education, and partly a matter of organisation and responsibility.

Mr. G. R. WILKINSON referred especially to steam under pressure as a sterilising agent. The equipment must allow the rapid displacement of air by steam at the start of the sterilisation cycle; it must allow condensate to escape; and the necessary temperature and pressure must be maintained for the necessary time.

Dr. J. C. KELSEY spoke of the difficulties of testing the bactericidal efficiency of steam sterilisers. Cultural tests had the advantage of being direct, but the results were obtained only slowly and skilled personnel were needed. Of the indirect methods, Browne's tubes probably represented the best routine test. Provision for recording thermometers should be made in all future steriliser installations, but as with the chemical tests they could not distinguish between moist heat and dry heat. Spore tests provided a useful check.

Dr. J. H. BOWIE hoped that hospital management would not neglect its responsibility for maintaining a proper environment. Encouragement and support must be given to the efforts of those who were doing their best with antiquated equipment in ill-designed and overcrowded buildings. As a pointer to the future, he described small trials of a device fitted to a steam steriliser which, by recirculating condensed steam at the end of the sterilisation cycle, trebled the rate of cooling of autoclaved bottles.

The proceedings are to be published by the Pharmaceutical Press.

University of Cambridge

On May 2 the following degrees were conferred:

M.D.—P. T. Annesley, I. R. McWhinney.
M.Chir.—J. D. Marsh, J. P. Williams, Cyril Shaldon (by proxy).
M.B.—D. D. Craig.

University of Dublin

Prof. W. J. E. Jessop has been appointed dean of the faculty of physic; and Dr. D. S. Torrens, dean since 1950, will become vice-dean and will continue to be concerned largely with the working administration of the school. Dr. G. W. Pennington has been appointed lecturer in pharmacology.

Royal College of Physicians of Edinburgh

At a meeting of the college on May 5, with Dr. J. D. S. Cameron, the vice-president, in the chair, the following were elected to the membership:

Robert Cruickshank, G. R. Hargreaves, J. H. Walters, A. J. S. McFadzean, K. W. Donald, M. A. Stewart, A. W. Woodruff, Nilakanta Sitaraman, Brajbansi Prasad, Arthur Daniel, Bankim Chandra Chattopadhaya, Mohamed Talaat El-Ghoneimy, Muniswamappa Ramu, Nalapat Kesava Menon, Joy D. G. Hobday, Jayakumar Nayar, C. B. S. Schofield, Elizabeth L. Brown, Veluppillai Rajapillai, R. A. Miller, F. W. Wigzell, Abul Khayer Khan, Canthavanam Chelliah Balasubramaniam, Mohamed Haniffa Mohamed Hamza, G. A. L.-G. Glazebrook, G. J. Green, Kali Prakash Dikshit, Sam Nariman, J. Yin Chi Pan, Malati Deshpande, Andrew Davis, C. M. Shugg, Subbian Chinnapullay, Khwaja Muin Ahmad, N. C. Allan, Mohan Pandurang Gollerkeri, R. J. Barnes, Sivakami Devi, Dennis Pittaway, P. S. Grero, J. D. Reid, I. C. Dunlop, G. M. Lewis, Mrigendra Raj Pandey, Rajpal Harbanslal Chhabra, Debabrata Gooptu, Sunil Kumar Sen, Chitaldroog Ramachandra Rao, Mahalekshmi Thangam Sushila, George Preswick, Binod Kumar Gupta, D. H. Friedlander, F. M. Elderkin, David Leak.

The Freeland Barbour fellowship has been awarded to A. F. Anderson.

Royal College of Surgeons of Edinburgh

At a meeting of the college on May 8, with Prof. John Bruce, the president, in the chair, the following were admitted to the fellowship:

Ajit Kumar Ahluwalia, Shedden Alexander, Dattatrya Manmohan Amonkar, John Anderson, Ali Farid Atawneh, Michel Tawfik Ayoub, C. E. Barth, J. N. Bear, Brijmohan Bhan, C. G. Bremner, Samarendra Chandra Chatterji, R. R. Cooke, E. P. Davison, Frederick Ehrlich, B. W. Fox, Kanwar Kuldip Singh Goleria, J. A. Gordon, A. N. Gorshenin, R. H. K. Gruneberg, A. H. Hackett, Lance Human, W. V. James, M. G. Jones, Kamal Vasudev Kasbekar, Ahmed Kazim, Theo Keldoulis, Satya Pal Kumar, Sumant Jayachand Kumbhani, J. G. Leitch, E. MacD. Little, D. M. McNab, M. R. Madigan, R. G. Mahaffy, W. G. C. Maling, Charles Malkin, Hans Raj Manchanda, I. A. Mansoor, Mini Hoshang Mehta, Victor Anomah Ngu, Mohamed Saad El Din Omar, D. C. Paterson, J. K. P. Perera, K. P. Robinson, Diyal Chand Sachdeva, J. S. Scott, D. G. Seaton, R. S. P. Sheedy, J. J. Shepherd, Robert Shields, Birendra Prasad Singh, Brajeshwar Singh, Doris Sohan-Lal, Louis Solomon, Charles Sorbie, D. W. Stuart, Calapatti Ramaswami Subramaniam, Maurice Sutton, T. K. F. Taylor, Ashok Maganlal Thakkar, Marx Wald, S. W. Willox, J. S. P. Wilson, Kean Seng Yeoh.

Royal Faculty of Physicians and Surgeons of Glasgow

On May 4 Robert Hume and Mohammed Naeem Sidiki were admitted to the fellowship, *qua* physician.

Overtime Payment for Doctors?

At a meeting on May 6 the South Worcestershire Hospital Management Committee discussed the shortage of housemen, and the consequent difficulty in maintaining a rota for casualty work and for minimal clinical duties. While recognising that doctors willingly accepted long hours as a feature of their professional life, the committee felt that where, as in this case, shortages were very protracted and had no clear term, arrangements should exist whereby some extra payment could be made for overtime worked by the hospital's own staff, or by staff of neighbouring hospitals whose help might then be more readily offered. It was agreed that strong representations to this effect be made to the regional hospital board.

Public Health and the Family Doctor

This is to be the subject of a joint conference, sponsored by the Wellcome Foundation, between the College of General Practitioners and the Society of Medical Officers of Health. The conference will open at 2.15 P.M. on Saturday, May 23, and will be concluded the following day.

Occupational Health Services

The International Labour Conference, meeting in Geneva on June 3 for its 43rd session, will consider a draft recommendation on occupational health services. This provides that these services should be organised by employers themselves or attached to an outside body, either as a separate service within a single undertaking or as a service common to a number of undertakings. It sees the role of the services as essentially preventive. The doctors in charge of them should enjoy full professional and moral independence from both employer and workers, and the services should not put the worker to expense.

Centenary Dinner of Royal Dental Hospital

Queen Elizabeth the Queen Mother, as chancellor of the University of London, attended the dinner held on May 8 to celebrate the centenary of the Royal Dental Hospital of London and its school of dental surgery. A message from the Queen, speaking of happiest recollections of her visit to the hospital last June, was read by Mr. C. Bowdler Henry, the senior surgeon, who presided. Other messages included one from the Baltimore College of Dental Surgery, mentioning that it was the oldest dental school in the world, and one from Mr. Warwick James.

Sir Wilfred Fish, president of the General Dental Council, said that nobody who had visited the school earlier in the day could have any doubt of its health—manifest in enthusiasm, gaiety, and a magnificent display of what can now be done for patients. By happy chance the opening of the new building last year had coincided with the celebration of the centenary, and since the school was actually opened on April 30, 1860, he looked forward to further celebrations next year. Everyone who went through the Royal Dental Hospital school was deeply in love with his alma mater, and it had a great tradition in research. John Tomes had been one of its founders; Warwick James had done some of the best research there at the beginning of this century; and the tradition was maintained by the dean and his coworkers.

Prof. R. B. Lucas, the dean, spoke of the investigations of Sir Wilfred Fish as an old member of the school. The new premises were a most welcome blood-transfusion, and, though the Ministry of Health was unable to proceed with entire rebuilding, the board of governors of St. George's Hospital (to which the Royal Dental Hospital is attached) had made all the improvements possible.

Viscountess Monckton, chairman of the hospital, proposing The Guests, mentioned among them Lord Ingleby, chairman of St. George's, and Mr. F. R. Moser, chosen to represent the old students of the school, and a generous benefactor for many years. Mr. W. R. Tattersall, president of the British Dental Association, responded.

British Orthoptic Board

At a dinner held by the board at Apothecaries Hall, London, on May 8, the toast of Orthoptics was proposed by Sir John Wolfenden, vice-chancellor of the University of Reading, who said that his family owed the profession a debt of profound gratitude. Responding for The Guests, Sir James Paterson Ross, P.R.C.S., spoke of the valuable part played by orthoptists during the war when many and varied conditions were treated in Servicemen.

Mr. A. B. Nott, chairman of the board, gave a brief history of the profession and said that it lacked sufficient new recruits. Miss D. N. Glenday, president of the Association of Headmistresses, promised more publicity in schools for the work of orthoptists, but thought that more should be done to enable orthoptists who married to obtain part-time work.

A documentary film *Orthoptics—A Career*, which is to be shown in schools as part of the recruitment campaign, was shown at the end of the dinner. This illustrates the 3-year course of training, and gives details of the opportunities after qualification.

Mr. Alan Hunt is visiting Poland, under the auspices of the British Council, at the invitation of the Polish Ministry of Health, to lecture in Warsaw and Cracow.

On April 26 the North-West England Faculty of the College of General Practitioners held in Manchester a symposium on coronary-artery disease in general practice. Prof. Robert Platt, P.R.C.P., was in the chair. Over 500 general practitioners were present, and over 100 applications for attendance had to be refused.

On Wednesday, May 27, at 8 P.M., the London Hospital is to hold a meeting of the hospital's consultants and of the general practitioners who use its services.

The next meeting at University College Hospital, London, for general practitioners will be held on Sunday, June 7, at 10.15 A.M. A clinical demonstration will be conducted by Prof. R. S. Pilcher, whose subject will be peripheral vascular disease.

At the annual meeting of the Louis Rapkine Association, held in London on May 4, it was announced that Dr. G. E. W. Wolstenholme has been awarded the Cross of Chevalier of the Legion of Honour in recognition of his work for international cooperation in medicine and science.

The Hypnotherapy Group will meet at 1, Wimpole Street, London, W.1, on Thursday, May 21, at 8 P.M., when there will be a brains trust.

CORRIGENDUM: *Potassium-secreting Tumours of the Large Intestine.*—In the second case mentioned by Mr. A. D. Roy and Mr. H. Ellis in the addendum to their article (April 11, p. 759) the units (stated in the addendum to be milli-equivalents per litre) were milligrammes per 100 ml.

Diary of the Week

MAY 17 TO 23

Tuesday, 19th

ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.1
5 P.M. Dr. Charles Pinckney: Care of the Premature Baby.

UNIVERSITY OF DUBLIN
4.30 P.M. (School of Physic, Trinity College.) Prof. R. J. V. Pulvertaft: The Lymphocyte in Malignant Disease. (John Mallet Purser lecture.)

Wednesday, 20th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5 P.M. *Comparative Medicine.* Mr. A. L. Ogden, Dr. Hermann Lehmann, Prof. Claude Rimington: Inherited Metabolic Characters in Man and Animals.
8.15 P.M. *General Practice.* Dame Ninette de Valois: British Ballet.

POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
2 P.M. Dr. B. W. Lacey: Environment and Microbial Antigens.

INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. R. S. F. Schilling: Recent Studies of Chronic Respiratory Disease in Cotton Workers.

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. Henry Haber: Eosinophilic Granuloma of the Skin.

EUGENICS SOCIETY
5.30 P.M. (Burlington House, Piccadilly, W.1.) Dr. Isabella Leitch, Dr. Angus Thomson: Growth, Heredity, and Nutrition.

UNIVERSITY OF LEEDS
5.15 P.M. (General Infirmary.) Dr. Peter Miescher (Basle): The Pathogenesis of Lupus Erythematosus.

Thursday, 21st

ROYAL SOCIETY OF MEDICINE
4.45 P.M. *Dermatology.* Dr. Stephen Gold, Dr. Miescher: Chronic Discoid Lupus Erythematosus.

POSTGRADUATE MEDICAL SCHOOL
4 P.M. Prof. W. J. H. Butterfield: Oral Preparations in the Treatment of Diabetes.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place, W.1
7.30 P.M. Dr. Ivan Polunin: The Muruts of North Borneo and Their Declining Population.

NUFFIELD ORTHOPÆDIC CENTRE, Wingfield-Morris Orthopædic Hospital, Oxford
8.30 P.M. Prof. Joseph Trueta: Reassessment of the Problem of Osteochondritis of the Hip.

HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Dr. M. B. Matthews: Observations on the Ætiology of Aortic Stenosis.

UNIVERSITY OF ST. ANDREWS
5 P.M. (Queen's College, Small's Wynd, Dundee.) Dr. R. G. Mitchell: Cerebral Palsy.

Friday, 22nd

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
5 P.M. Lord Cohen of Birkenhead: Facial Neuralgias. (Charles Tomes lecture.)

ROYAL SOCIETY OF MEDICINE
5 P.M. *Pædiatrics.* Prof. Douglas Hubble, Dr. Alice Stewart, Prof. G. M. Wilson, Dr. Cedric Carter: Problems of Irradiation in Childhood.
5.30 P.M. *Epidemiology and Preventive Medicine.* Mr. S. Rosenbaum: Cross-sectional Review of Morbidity Amongst Young Soldiers.
8.15 P.M. *Obstetrics and Gynæcology.* Sir Archibald McIndoe, Mr. C. A. Simmons, Mr. F. W. Roques, Dr. C. Seah: Treatment of Congenital Absence of Vagina with Emphasis on Long-term Results.

POSTGRADUATE MEDICAL SCHOOL
10 A.M. Mr. Clifford Jones: Vasomotor Disturbances of the Hands.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
5.30 P.M. Mr. Maxwell Ellis: The Theory of Voice Production.